

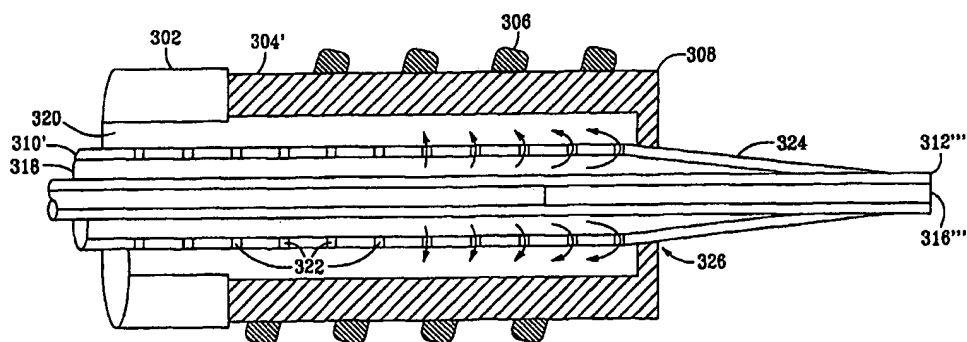


15

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61M 1/36, A61F 7/12		A1	(11) International Publication Number: WO 99/66971
		(43) International Publication Date: 29 December 1999 (29.12.99)	
(21) International Application Number: PCT/US99/14257		(81) Designated States: AU, CA, JP, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).	
(22) International Filing Date: 22 June 1999 (22.06.99)			
(30) Priority Data:		Published <i>With international search report.</i>	
09/103,342	23 June 1998 (23.06.98) US		
09/215,038	16 December 1998 (16.12.98) US		
09/215,039	16 December 1998 (16.12.98) US		
09/232,177	15 January 1999 (15.01.99) US		
09/246,788	9 February 1999 (09.02.99) US		
(71) Applicant: DEL MAR MEDICAL TECHNOLOGIES, INC. [US/US]; Suite 106, 6199 Cornerstone Court East, San Diego, CA 92121 (US).			
(72) Inventors: DOBAK, John, D., III; 2385 Ridgeway Row, La Jolla, CA 92037 (US). LASHERAS, Juan, C.; 6898 Via Estrada, La Jolla, CA 92037 (US). WERNETH, Randall, L.; 3868 Arverne Street, San Diego, CA 92111 (US).			
(74) Agents: BEUERLE, Stephen, C. et al.; Lyon & Lyon LLP, Suite 4700, 633 West Fifth Street, Los Angeles, CA 90071-2066 (US).			

(54) Title: METHOD AND DEVICE FOR APPLICATIONS OF SELECTIVE ORGAN COOLING



(57) Abstract

The invention provides a method and device for heating or cooling a surrounding fluid in a feeding vessel. The device includes a catheter assembly capable of insertion to a selected feeding vessel in the vascular system of a patient. The assembly includes a heat transfer element at a distal end of the catheter assembly, the heat transfer element (14) having a plurality of exterior surface irregularities (20, 24) shaped and arranged to create turbulence in a surrounding fluid, the surface irregularities (20, 24) having a depth at least equal to the boundary layer thickness of flow of the surrounding fluid in the feeding vessel. The assembly also includes a supply catheter (12) to deliver a working fluid to an interior of the heat transfer element (14), a return catheter (202) to return a working fluid from the interior of the heat transfer element (14), and a drug delivery catheter (312) running substantially parallel to the axis of the catheter assembly.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

TITLE OF THE INVENTION

Method and Device for Applications of Selective Organ Cooling

BACKGROUND OF THE INVENTION

Field of the Invention - The present invention relates generally to the
5 modification and control of the temperature of a selected body organ. More
particularly, the invention relates to applications of selective organ cooling which
advantageously employ complementary techniques.

Background Information - Organs in the human body, such as the brain, kidney
and heart, are maintained at a constant temperature of approximately 37°C.
10 Hypothermia can be clinically defined as a core body temperature of 35°C or less.
Hypothermia is sometimes characterized further according to its severity. A body core
temperature in the range of 33°C to 35°C is described as mild hypothermia. A body
temperature of 28°C to 32°C is described as moderate hypothermia. A body core
temperature in the range of 24°C to 28°C is described as severe hypothermia.

15 Hypothermia is uniquely effective in reducing brain injury caused by a variety
of neurological insults and may eventually play an important role in emergency brain
resuscitation. Experimental evidence has demonstrated that cerebral cooling improves
outcome after global ischemia, focal ischemia, or traumatic brain injury. For this
reason, hypothermia may be induced in order to reduce the effect of certain bodily
20 injuries to the brain as well as other organs.

Cerebral hypothermia has traditionally been accomplished through whole body
cooling to create a condition of total body hypothermia in the range of 20°C to 30°C.
However, the use of total body hypothermia risks certain deleterious systematic
vascular effects. For example, total body hypothermia may cause severe derangement
25 of the cardiovascular system, including low cardiac output, elevated systematic
resistance, and ventricular fibrillation. Other side effects include renal failure,
disseminated intravascular coagulation, and electrolyte disturbances. In addition to the
undesirable side effects, total body hypothermia is difficult to administer.

Catheters have been developed which are inserted into the bloodstream of the
30 patient in order to induce total body hypothermia. For example, U.S. Patent No.
3,425,419 to Dato describes a method and apparatus of lowering and raising the

temperature of the human body. Dato induces moderate hypothermia in a patient using a metallic catheter. The metallic catheter has an inner passageway through which a fluid, such as water, can be circulated. The catheter is inserted through the femoral vein and then through the inferior vena cava as far as the right atrium and the superior vena cava. The Dato catheter has an elongated cylindrical shape and is constructed from stainless steel. By way of example, Dato suggests the use of a catheter approximately 70 cm in length and approximately 6 mm in diameter. However, use of the Dato device implicates the negative effects of total body hypothermia described above.

Due to the problems associated with total body hypothermia, attempts have been made to provide more selective cooling. For example, cooling helmets or headgear have been used in an attempt to cool only the head rather than the patient's entire body. However, such methods rely on conductive heat transfer through the skull and into the brain. One drawback of using conductive heat transfer is that the process of reducing the temperature of the brain is prolonged. Also, it is difficult to precisely control the temperature of the brain when using conduction due to the temperature gradient that must be established externally in order to sufficiently lower the internal temperature. In addition, when using conduction to cool the brain, the face of the patient is also subjected to severe hypothermia, increasing discomfort and the likelihood of negative side effects. It is known that profound cooling of the face can cause similar cardiovascular side effects as total body cooling. From a practical standpoint, such devices are cumbersome and may make continued treatment of the patient difficult or impossible.

Selected organ hypothermia has been accomplished using extracorporeal perfusion, as detailed by Arthur E. Schwartz, M.D. et al., in *Isolated Cerebral Hypothermia by Single Carotid Artery Perfusion of Extracorporeally Cooled Blood in Baboons*, which appeared in Vol. 39, No. 3, NEUROSURGERY 577 (September, 1996). In this study, blood was continually withdrawn from baboons through the femoral artery. The blood was cooled by a water bath and then infused through a common carotid artery with its external branches occluded. Using this method, normal heart rhythm, systemic arterial blood pressure and arterial blood gas values were maintained during the hypothermia. This study showed that the brain could be selectively cooled to temperatures of 20° C without reducing the temperature of the entire body. However,

external circulation of blood is not a practical approach for treating humans because the risk of infection, need for anticoagulation, and risk of bleeding is too great. Further, this method requires cannulation of two vessels making it more cumbersome to perform particularly in emergency settings. Even more, percutaneous cannulation of the carotid artery is difficult and potentially fatal due to the associated arterial wall trauma. Finally, this method would be ineffective to cool other organs, such as the kidneys, because the feeding arteries cannot be directly cannulated percutaneously.

Selective organ hypothermia has also been attempted by perfusion of a cold solution such as saline or perfluorocarbons. This process is commonly used to protect the heart during heart surgery and is referred to as cardioplegia. Perfusion of a cold solution has a number of drawbacks, including a limited time of administration due to excessive volume accumulation, cost, and inconvenience of maintaining the perfusate and lack of effectiveness due to the temperature dilution from the blood. Temperature dilution by the blood is a particular problem in high blood flow organs such as the brain.

BRIEF SUMMARY OF THE INVENTION

The invention provides a practical method and apparatus which modifies and controls the temperature of a selected organ and which may be used in combination with many complementary therapeutic techniques.

In one aspect, the invention is directed towards a device for heating or cooling a surrounding fluid in a feeding vessel. The device includes a catheter assembly capable of insertion to a selected feeding vessel in the vascular system of a patient. The assembly includes a heat transfer element at a distal end of the catheter assembly, the heat transfer element having a plurality of exterior surface irregularities shaped and arranged to create turbulence in a surrounding fluid, the surface irregularities having a depth at least equal to the boundary layer thickness of flow of the surrounding fluid in the feeding vessel. The surrounding fluid may be, e.g., blood in a blood vessel, working fluid within the heat transfer element, etc., and combinations thereof. The assembly further includes a supply catheter to deliver a working fluid to an interior of the heat transfer element and a return catheter to return a working fluid from the interior of the heat transfer element. A drug delivery catheter is also provided and runs substantially parallel to the axis of the catheter assembly.

Implementations of the invention may include one or more of the following.

The drug delivery catheter may be disposed substantially coaxially with respect to the supply catheter. The drug delivery catheter may include an outlet at a distal end thereof, the distal end of the drug delivery catheter distal of a distal end of the return or
5 supply catheters. The drug delivery catheter may be disposed within one of the return catheter or the supply catheter or both, and may include an outlet transverse or parallel to the axis of the catheter assembly. The surface irregularities may include a helical ridge and a helical groove formed on each of successive heat transfer segments; and the helical ridge on each heat transfer segment may have an opposite helical twist to the
10 helical ridges on adjacent heat transfer segments. At least one sealed lumen within one of the return catheter or the supply catheter or both may be provided, the sealed lumen in pressure communication with a supply of air to inflate the sealed lumen. The return catheter may be coaxial with the supply catheter, and the return catheter have a larger or smaller radius than the supply catheter, depending on the requirements of the user.

15 In another aspect, the invention is directed to a device for heating or cooling a surrounding fluid in a feeding vessel. In this aspect, the heat transfer element has a distal end which defines an orifice. A supply catheter deliver a working fluid to an interior of the heat transfer element, the supply catheter having a working fluid catheter disposed therein and further having disposed therein a drug delivery catheter running
20 substantially parallel to the axis of the supply catheter. The working fluid catheter has defined thereon a number of outlets to communicate the working fluid from the interior of the supply catheter to a volume defined by the exterior of the supply catheter and the interior of the heat transfer element. The device further includes a return catheter to return the working fluid from the interior of the heat transfer element.

25 In yet another aspect, the invention is directed to a method for selectively controlling the temperature of a selected volume of blood in a patient. The method includes introducing a catheter assembly into a blood vessel feeding a selected volume of blood in a patient, and delivering a working fluid through a supply catheter in the catheter assembly and returning the working fluid through a return catheter in the
30 catheter assembly. Heat is transferred between a heat transfer element forming a distal end of the catheter assembly and the volume of blood in the feeding vessel. A liquid is delivered through a drug delivery catheter to the volume of blood in the feeding vessel.

Implementations of the invention may include one or more of the following. Turbulence may be created around a plurality of surface irregularities on the heat transfer element at a distance from the heat transfer element greater than the boundary layer thickness of flow in the feeding vessel, thereby creating turbulence throughout a free stream of blood flow in the feeding vessel. The surface irregularities on the heat transfer element may include a plurality of segments of helical ridges and grooves having alternating directions of helical rotation; and turbulence is created by establishing repetitively alternating directions of helical blood flow with the alternating helical rotations of the ridges and grooves. The liquid may be a warm enzyme solution, and may be selected from the group consisting of tPA, streptokinase, urokinase, pro-urokinase, and combinations thereof. The liquid may be delivered to the volume in a longitudinal or transverse direction with respect to the axis of the catheter assembly. The liquid may be delivered to the volume proximal or distal of the distal tip of the catheter assembly. If the volume of blood includes a blood clot, during the delivering of the liquid the distal tip of the catheter assembly may be disposed substantially near, adjacent, or embedded in the blood clot. Air may be delivered to at least one sealed lumen within the return catheter to cause the sealed lumen to enlarge. The air may further be delivered in a pulsatile fashion to repeatedly enlarge and contract the sealed lumen, thereby to create additional turbulence, e.g., to enhance heat transfer.

A further aspect of the invention involves method for selectively controlling the temperature of a selected volume of blood in a patient. The method includes introducing a catheter assembly into a blood vessel feeding a selected volume of blood in a patient; delivering a working fluid through a supply catheter in the catheter assembly and returning the working fluid through a return catheter in the catheter assembly; transferring heat between a heat transfer element forming a distal end of the catheter assembly and the volume of blood in the feeding vessel; and delivering a liquid through a drug delivery catheter to the volume of blood in the feeding vessel.

In an embodiment of the above aspect of the invention, the method further includes creating turbulence around a plurality of surface irregularities on the heat transfer element at a distance from the heat transfer element greater than the boundary layer thickness of flow in the feeding vessel, thereby creating turbulence throughout a free stream of blood flow in the feeding vessel.

In another embodiment of the above aspect of the invention, surface irregularities on the heat transfer element comprise a plurality of segments of helical ridges and grooves having alternating directions of helical rotation; and turbulence is created by establishing repetitively alternating directions of helical blood flow with the alternating helical rotations of the ridges and grooves.

In a further embodiment of the above aspect of the invention, the liquid is a warm enzyme solution.

In a still further embodiment of the above aspect of the invention, the warm enzyme solution is selected from the group consisting of tPA, streptokinase, urokinase, pro-urokinase, and combinations thereof.

In an additional embodiment of the above aspect of the invention, the method further includes delivering air to at least one sealed lumen within the return catheter to cause the sealed lumen to enlarge.

In a further embodiment of the above aspect of the invention, the method further includes delivering air in a pulsatile fashion to the at least one sealed lumen within the return catheter to cause the sealed lumen to repeatedly enlarge and contract.

In a still further embodiment of the above aspect of the invention, the method further includes delivering the liquid to the volume in a longitudinal direction with respect to the axis of the catheter assembly.

In an additional embodiment of the above aspect of the invention, the method further includes delivering the liquid to the volume in a transverse direction with respect to the axis of the catheter assembly.

In another embodiment of the above aspect of the invention, delivering the liquid to the volume distal of the distal tip of the catheter assembly.

In a further embodiment of the above aspect of the invention, the volume of blood includes a blood clot, and during the delivering the liquid the distal tip of the catheter assembly is substantially near, adjacent, or embedded in the blood clot.

In a still further embodiment of the above aspect of the invention, the method further includes delivering the liquid proximal of the distal tip of the catheter assembly.

Advantages of the invention include the following. The device may be placed in an artery without traumatizing the arterial wall and with damaging the device itself. The device may be placed in an artery simply and by a variety of practitioners such as cardiologists or neurosurgeons. The device allows the complementary performance of

simultaneous procedures along with brain cooling, these procedures including angiography, stenotic lesion stenting, and drug delivery.

A still further aspect of the invention involves a method for selectively controlling the temperature of a selected organ of a patient for performance of a specified application. The method includes introducing a guide catheter into a blood vessel; providing a supply tube having a heat transfer element attached to a distal end thereof, the heat transfer element having a plurality of exterior surface irregularities, the surface irregularities having a depth greater than the boundary layer thickness of flow in the feeding artery of the selected organ; inserting the supply tube and heat transfer element through the guide catheter to place the heat transfer element in the feeding artery of the selected organ; creating turbulence around the surface irregularities at a distance from the heat transfer element greater than the boundary layer thickness of flow in the feeding artery, thereby creating turbulence throughout the blood flow in the feeding artery; circulating fluid into the heat transfer element via the supply tube; circulating fluid out of the heat transfer element via the guide catheter; and transferring heat between the heat transfer element and the blood in the feeding artery to selectively control the temperature of the selected organ.

In an embodiment of the above aspect of the invention, the surface irregularities on the heat transfer element comprise a plurality of segments of helical ridges and grooves having alternating directions of helical rotation; and turbulence is created by establishing repetitively alternating directions of helical blood flow with the alternating helical rotations of the ridges and grooves.

In an additional embodiment of the above aspect of the invention, the method further includes inducing blood turbulence in greater than 20% of the period of the cardiac cycle within the carotid artery.

A further aspect of the invention involves a method for selective thrombolysis by selective vessel hypothermia. The method includes introducing a guide catheter into a thrombosed blood vessel; delivering a thrombolytic drug to the blood by flowing the thrombolytic drug into the guide catheter; introducing a supply tube having a heat transfer element at a distal end thereof into the thrombosed blood vessel through the guide catheter; cooling the heat transfer element by flowing a working fluid through the heat transfer element, the return path for the working fluid being the guide catheter; and

cooling the blood by flowing the blood past the heat transfer element, such that the blood is cooled to a prespecified temperature range.

In an embodiment of the above aspect of the invention, the drug is chosen from the group consisting of tPA, urokinase, streptokinase, precursors of urokinase, and combinations thereof.

In an additional embodiment of the above aspect of the invention, the thrombolytic drug is streptokinase and the prespecified temperature range is between about 30°C and 32°C.

In another embodiment of the above aspect of the invention, the thrombolytic drug is urokinase and the prespecified temperature range is below about 28°C.

In a further embodiment of the above aspect of the invention, the thrombolytic drug is a precursor to urokinase and the prespecified temperature range is below about 28°C.

Another aspect of the invention involves a method for selective thrombolysis by selective vessel hyperthermia. The method includes introducing a guide catheter into a thrombosed blood vessel; delivering a thrombolytic drug to the blood by flowing the thrombolytic drug into the guide catheter; introducing a supply tube having a heat transfer element at a distal end thereof into the thrombosed blood vessel through the guide catheter; heating the heat transfer element by flowing a working fluid through the heat transfer element, the return path for the working fluid being the guide catheter; and heating the blood by flowing the blood past the heat transfer element, such that the blood is heated to a prespecified temperature range.

In an embodiment of the above aspect of the invention, the drug is chosen from the group consisting of tPA, urokinase, streptokinase, precursors of urokinase, and combinations thereof.

In an additional embodiment of the above aspect of the invention, the drug is tPA and the prespecified temperature range is between about 37°C to 40°C.

A further aspect of the invention involves a method for performing angiography during selective vessel hypothermia. The method includes introducing a guide catheter into a blood vessel; delivering a radioopaque fluid to the blood by flowing the radioopaque fluid into the guide catheter; introducing a supply tube having a heat transfer element at a distal end thereof into the blood vessel through the guide catheter; cooling the heat transfer element by flowing a working fluid through the heat transfer

element, the return path for the working fluid being the guide catheter; and cooling the blood by flowing the blood past the heat transfer element, such that the blood is cooled to a prespecified temperature range.

5 A still further aspect of the invention involves a method for performing stenting of a stenotic lesion during selective vessel hypothermia. The method includes introducing a guide catheter into a blood vessel; introducing a guide wire through the guide catheter and across a stenotic lesion; delivering a balloon catheter loaded with a stent via the guide wire; positioning the stent across the lesion; expanding the balloon with contrast; deploying the stent; introducing a supply tube having a heat transfer
10 element at a distal end thereof into the blood vessel through the guide catheter; cooling the heat transfer element by flowing a working fluid through the heat transfer element, the return path for the working fluid being the guide catheter; and cooling the blood by flowing the blood past the heat transfer element, such that the blood is cooled to a prespecified temperature range.

15 An additional aspect of the invention involves a method for selectively controlling the temperature of a selected organ of a patient for performance of a specified application. The method includes introducing a return catheter into a blood vessel having a heat transfer element attached to a distal end thereof, the heat transfer element having a plurality of exterior surface irregularities, the surface irregularities
20 having a depth greater than the boundary layer thickness of flow in the feeding artery of the selected organ, the heat transfer element having an outlet at a distal end thereof; inserting a working fluid catheter into the return catheter and heat transfer element such that the working fluid catheter plugs the outlet of the heat transfer element; creating turbulence around the surface irregularities at a distance from the heat transfer element
25 greater than the boundary layer thickness of flow in the feeding artery, thereby creating turbulence throughout the blood flow in the feeding artery; circulating fluid into the heat transfer element via the working fluid catheter; circulating fluid out of the heat transfer element via the return catheter; and transferring heat between the heat transfer element and the blood in the feeding artery to selectively control the temperature of the
30 selected organ.

In an embodiment of the above aspect of the invention, the method further includes removing the working fluid catheter from the return catheter and the heat transfer element; inserting a delivery catheter into the return catheter and the heat

transfer element, the delivery catheter having a delivery outlet at a distal end thereof; and delivering a drug via the delivery catheter.

In an additional embodiment of the above aspect of the invention, the surface irregularities on the heat transfer element comprise a plurality of segments of helical ridges and grooves having alternating directions of helical rotation; and turbulence is created by establishing repetitively alternating directions of helical blood flow with the alternating helical rotations of the ridges and grooves.

A further aspect of the invention involves a method for selectively controlling the temperature of a selected organ of a patient for performance of a specified application. The method includes introducing a return catheter into a blood vessel having a heat transfer element attached to a distal end thereof, the heat transfer element having a plurality of exterior surface irregularities, the surface irregularities having a depth greater than the boundary layer thickness of flow in the feeding artery of the selected organ, the heat transfer element having an outlet at a distal end thereof; inserting a delivery / working fluid catheter into the return catheter and heat transfer element such that the delivery / working fluid catheter plugs the outlet of the heat transfer element in a first condition and an inflatable balloon coupled to a distal end of the delivery / working fluid catheter plugs the outlet of the heat transfer element in a second condition, the delivery / working fluid catheter having a delivery outlet at the distal end thereof and at least one working fluid outlets at a distance upstream of the distal end; creating turbulence around the surface irregularities at a distance from the heat transfer element greater than the boundary layer thickness of flow in the feeding artery, thereby creating turbulence throughout the blood flow in the feeding artery; in the first condition, circulating fluid into the heat transfer element via the working fluid catheter; circulating fluid out of the heat transfer element via the return catheter; and transferring heat between the heat transfer element and the blood in the feeding artery to selectively control the temperature of the selected organ; and in the second condition, delivering a drug to the blood via the delivery outlet in the first condition.

The novel features of this invention, as well as the invention itself, will be best understood from the attached drawings, taken along with the following description, in which similar reference characters refer to similar parts, and in which:

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

Figure 1 is a front view of a first embodiment of a turbulence inducing heat transfer element according to the principles of the invention within an artery;

Figure 2 is a more detailed front view of the heat transfer element of Figure 1;

5 Figure 3 is a front sectional view of the heat transfer element of Figure 1;

Figure 4 is a transverse sectional view of the heat transfer element of Figure 1;

Figure 5 is a front perspective view of the heat transfer element of Figure 1 in use within a partially broken away blood vessel;

10 Figure 6 is a partially broken away front perspective view of a second embodiment of a turbulence inducing heat transfer element according to the principles of the invention;

Figure 7 is a transverse sectional view of the heat transfer element of Figure 6;

Figure 8 is a schematic representation of the invention being used to cool the brain of a patient;

15 Figure 9 is a front sectional view of a guide catheter according to an embodiment of the invention which may be employed for applications of the heat transfer element according to the principles of the invention;

20 Figure 10 is a front sectional view of a third embodiment of a catheter employing a heat transfer element according to the principles of the invention further employing a return tube / guide catheter;

Figure 11 is a front sectional view of a fourth embodiment of a catheter employing a heat transfer element according to the principles of the invention further employing a delivery catheter;

25 Figure 12 is a front sectional view of the fourth embodiment of Figure 11 further employing a working fluid catheter;

Figure 13 is a front sectional view of a fifth embodiment of a catheter employing a heat transfer element according to the principles of the invention further employing a guide wire;

30 Figure 14 is a front sectional view of a sixth embodiment of a catheter employing a heat transfer element according to the principles of the invention further employing a delivery / working fluid catheter with a balloon attachment;

Figure 15 is a second front sectional view of the sixth embodiment of Figure 14 shown with the balloon attachment occluding an opening in the heat transfer element;

Figure 16 is a front sectional view of a seventh embodiment of a catheter employing a heat transfer element according to the principles of the invention further employing a delivery lumen;

Figure 17 is a front sectional view of an eighth embodiment of a catheter
5 employing a heat transfer element according to the principles of the invention further employing a delivery lumen, this delivery lumen non-coaxial with the central body of the catheter;

Figure 18 is a front sectional view of a ninth embodiment of a catheter employing a heat transfer element according to the principles of the invention further
10 employing a delivery lumen, this delivery lumen non-coaxial with the central body of the catheter;

Figure 19 is a front sectional view of a tenth embodiment of a catheter employing a heat transfer element according to the principles of the invention further employing multiple lumens;

Figure 20 is a cross-sectional view of the tenth embodiment of Figure 19, taken
15 along lines 20-20 of Figure 19; and

Figure 21 is a front sectional view of an eleventh embodiment of a catheter employing a heat transfer element according to the principles of the invention.

20 DETAILED DESCRIPTION OF THE INVENTION

The temperature of a selected organ may be intravascularly regulated by a heat transfer element placed in the organ's feeding artery to absorb or deliver heat to or from the blood flowing into the organ. While the method is described with respect to blood flow into an organ, it is understood that heat transfer within a volume of tissue is
25 analogous. In the latter case, heat transfer is predominantly by conduction.

The heat transfer may cause either a cooling or a heating of the selected organ. A heat transfer element that selectively alters the temperature of an organ should be capable of providing the necessary heat transfer rate to produce the desired cooling or heating effect within the organ to achieve a desired temperature.

30 The heat transfer element should be small and flexible enough to fit within the feeding artery while still allowing a sufficient blood flow to reach the organ in order to avoid ischemic organ damage. Feeding arteries, like the carotid artery, branch off the aorta at various levels. Subsidiary arteries continue to branch off these initial branches.

For example, the internal carotid artery branches off the common carotid artery near the angle of the jaw. The heat transfer element is typically inserted into a peripheral artery, such as the femoral artery, using a guide catheter or guide wire, and accesses a feeding artery by initially passing through a series of one or more of these branches. Thus, the flexibility and size, e.g., the diameter, of the heat transfer element are important characteristics. This flexibility is achieved as is described in more detail below.

These points are illustrated using brain cooling as an example. The common carotid artery supplies blood to the head and brain. The internal carotid artery branches off the common carotid artery to supply blood to the anterior cerebrum. The heat transfer element may be placed into the common carotid artery or into both the common carotid artery and the internal carotid artery.

The benefits of hypothermia described above are achieved when the temperature of the blood flowing to the brain is reduced to between 30°C and 32°C. A typical brain has a blood flow rate through each carotid artery (right and left) of approximately 250-375 cubic centimeters per minute (cc/min). With this flow rate, calculations show that the heat transfer element should absorb approximately 75-175 watts of heat when placed in one of the carotid arteries to induce the desired cooling effect. Smaller organs may have less blood flow in their respective supply arteries and may require less heat transfer, such as about 25 watts.

The method employs conductive and convective heat transfers. Once the materials for the device and a working fluid are chosen, the conductive heat transfers are solely dependent on the temperature gradients. Convective heat transfers, by contrast, also rely on the movement of fluid to transfer heat. Forced convection results when the heat transfer surface is in contact with a fluid whose motion is induced (or forced) by a pressure gradient, area variation, or other such force. In the case of arterial flow, the beating heart provides an oscillatory pressure gradient to force the motion of the blood in contact with the heat transfer surface. One of the aspects of the device uses turbulence to enhance this forced convective heat transfer.

The rate of convective heat transfer Q is proportional to the product of S , the area of the heat transfer element in direct contact with the fluid, $\Delta T = T_b - T_s$, the temperature differential between the surface temperature T_s of the heat transfer element and the free stream blood temperature T_b , and \bar{h}_c , the average convection heat

transfer coefficient over the heat transfer area. \bar{h}_c is sometimes called the "surface coefficient of heat transfer" or the "convection heat transfer coefficient".

The magnitude of the heat transfer rate Q to or from the fluid flow can be increased through manipulation of the above three parameters. Practical constraints
 5 limit the value of these parameters and how much they can be manipulated. For example, the internal diameter of the common carotid artery ranges from 6 to 8 mm. Thus, the heat transfer element residing therein may not be much larger than 4 mm in diameter to avoid occluding the vessel. The length of the heat transfer element should also be limited. For placement within the internal and common carotid artery, the
 10 length of the heat transfer element is limited to about 10 cm. This estimate is based on the length of the common carotid artery, which ranges from 8 to 12 cm.

Consequently, the value of the surface area S is limited by the physical constraints imposed by the size of the artery into which the device is placed. Surface features, such as fins, can be used to increase the surface area of the heat transfer
 15 element, however, these features alone cannot provide enough surface area enhancement to meet the required heat transfer rate to effectively cool the brain.

One may also attempt to vary the magnitude of the heat transfer rate by varying ΔT . The value of $\Delta T = T_b - T_s$ can be varied by varying the surface temperature T_s of the heat transfer element. The allowable surface temperature of the heat transfer
 20 element is limited by the characteristics of blood. The blood temperature is fixed at about 37°C, and blood freezes at approximately 0°C. When the blood approaches freezing, ice emboli may form in the blood which may lodge downstream, causing serious ischemic injury. Furthermore, reducing the temperature of the blood also increases its viscosity which results in a small decrease in the value of \bar{h}_c . Increased
 25 viscosity of the blood may further result in an increase in the pressure drop within the artery, thus compromising the flow of blood to the brain. Given the above constraints, it is advantageous to limit the surface temperature of the heat transfer element to approximately 1°C - 5°C, thus resulting in a maximum temperature differential between the blood stream and the heat transfer element of approximately 32°C - 36°C.

30 One may also attempt to vary the magnitude of the heat transfer rate by varying \bar{h}_c . Fewer constraints are imposed on the value of the convection heat transfer coefficient \bar{h}_c . The mechanisms by which the value of \bar{h}_c may be increased are

complex. However, one way to increase \overline{h}_c for a fixed mean value of the velocity is to increase the level of turbulent kinetic energy in the fluid flow.

The heat transfer rate $Q_{\text{no-flow}}$ in the absence of fluid flow is proportional to ΔT , the temperature differential between the surface temperature T_s of the heat transfer
 5 element and the free stream blood temperature T_b , times k , the diffusion constant, and is inversely proportion to δ , the thickness of the boundary layer.

The magnitude of the enhancement in heat transfer by fluid flow can be estimated by taking the ratio of the heat transfer rate with fluid flow to the heat transfer rate in the absence of fluid flow $N = Q_{\text{flow}} / Q_{\text{no-flow}} = \overline{h}_c / (k/\delta)$. This ratio is called the
 10 Nusselt number ("Nu"). For convective heat transfer between blood and the surface of the heat transfer element, Nusselt numbers of 50-80 have been found to be appropriate for selective cooling applications of various organs in the human body. Nusselt numbers are generally dependent on several other numbers: the Reynolds number, the Womersley number, and the Prandtl number.

15 Stirring-type mechanisms, which abruptly change the direction of velocity vectors, may be utilized to induce turbulent kinetic energy and increase the heat transfer rate. The level of turbulence so created is characterized by the turbulence intensity θ . Turbulence intensity θ is defined as the root mean square of the fluctuating velocity divided by the mean velocity. Such mechanisms can create high levels of turbulence
 20 intensity in the free stream, thereby increasing the heat transfer rate. This turbulence intensity should ideally be sustained for a significant portion of the cardiac cycle, and should ideally be created throughout the free stream and not just in the boundary layer.

Turbulence does occur for a short period in the cardiac cycle anyway. In particular, the blood flow is turbulent during a small portion of the descending systolic
 25 flow. This portion is less than 20% of the period of the cardiac cycle. If a heat transfer element is placed co-axially inside the artery, the heat transfer rate will be enhanced during this short interval. For typical of these fluctuations, the turbulence intensity is at least 0.05. In other words, the instantaneous velocity fluctuations deviate from the mean velocity by at least 5%. In some embodiments, lower fluctuations may be
 30 employed, such as 3% or even 2%. Although ideally turbulence is created throughout the entire period of the cardiac cycle, the benefits of turbulence are obtained if the

turbulence is sustained for 75%, 50% or even as low as 30% or 20% of the cardiac cycle.

One type of turbulence-inducing heat transfer element which may be advantageously employed is a heat transfer element made of a high thermal conductivity material, such as metal. The use of a high thermal conductivity material increases the heat transfer rate for a given temperature differential between the coolant within the heat transfer element and the blood. This facilitates the use of a higher temperature coolant within the heat transfer element, allowing safer coolants, such as water, to be used. Highly thermally conductive materials, such as metals, tend to be rigid. In that application, bellows provided a high degree of articulation that compensated for the intrinsic stiffness of the metal. In another application, the bellows are replaced with a straight metal tube having a predetermined thickness to allow flexibility via bending of the metal. Alternatively, the bellows may be replaced with a polymer tube, *e.g.*, a latex rubber tube, a plastic tube, or a flexible plastic corrugated tube.

The device size may be minimized, *e.g.*, less than 4 mm, to prevent blockage of the blood flowing in the artery. The design of the heat transfer element should facilitate flexibility in an inherently inflexible material.

To create the desired level of turbulence intensity in the blood free stream during the whole cardiac cycle, one embodiment of the device uses a modular design. This design creates helical blood flow and produces a high level of turbulence in the free stream by periodically forcing abrupt changes in the direction of the helical blood flow. Figure 1 is a perspective view of such a turbulence inducing heat transfer element within an artery. Turbulent flow would be found at point 114, in the free stream area. The abrupt changes in flow direction are achieved through the use of a series of two or more heat transfer segments, each comprised of one or more helical ridges. To affect the free stream, the depth of the helical ridge is larger than the thickness of the boundary layer which would develop if the heat transfer element had a smooth cylindrical surface.

The use of periodic abrupt changes in the helical direction of the blood flow in order to induce strong free stream turbulence may be illustrated with reference to a common clothes washing machine. The rotor of a washing machine spins initially in one direction causing laminar flow. When the rotor abruptly reverses direction,

significant turbulent kinetic energy is created within the entire wash basin as the changing currents cause random turbulent motion within the clothes-water slurry.

Figure 2 is an elevation view of one embodiment of a heat transfer element 14. The heat transfer element 14 is comprised of a series of elongated, articulated segments or modules 20, 22, 24. Three such segments are shown in this embodiment, but two or
5 more such segments could be used. As seen in Figure 2, a first elongated heat transfer segment 20 is located at the proximal end of the heat transfer element 14. A turbulence-inducing exterior surface of the segment 20 comprises four parallel helical ridges 28 with four parallel helical grooves 26 therebetween. One, two, three, or more
10 parallel helical ridges 28 could also be used. In this embodiment, the helical ridges 28 and the helical grooves 26 of the heat transfer segment 20 have a left hand twist, referred to herein as a counter-clockwise spiral or helical rotation, as they proceed toward the distal end of the heat transfer segment 20.

The first heat transfer segment 20 is coupled to a second elongated heat transfer
15 segment 22 by a first tube section 25, which provides flexibility. The second heat transfer segment 22 comprises one or more helical ridges 32 with one or more helical grooves 30 therebetween. The ridges 32 and grooves 30 have a right hand, or clockwise, twist as they proceed toward the distal end of the heat transfer segment 22. The second heat transfer segment 22 is coupled to a third elongated heat transfer
20 segment 24 by a second tube section 27. The third heat transfer segment 24 comprises one or more helical ridges 36 with one or more helical grooves 34 therebetween. The helical ridge 36 and the helical groove 34 have a left hand, or counter-clockwise, twist as they proceed toward the distal end of the heat transfer segment 24. Thus, successive heat transfer segments 20, 22, 24 of the heat transfer element 14 alternate between
25 having clockwise and counterclockwise helical twists. The actual left or right hand twist of any particular segment is immaterial, as long as adjacent segments have opposite helical twist.

In addition, the rounded contours of the ridges 28, 32, 36 also allow the heat transfer element 14 to maintain a relatively atraumatic profile, thereby minimizing the
30 possibility of damage to the blood vessel wall. A heat transfer element may be comprised of two, three, or more heat transfer segments.

The tube sections 25, 27 are formed from seamless and nonporous materials, such as metal, and therefore are impermeable to gas, which can be particularly

important, depending on the type of working fluid that is cycled through the heat transfer element 14. The structure of the tube sections 25, 27 allows them to bend, extend and compress, which increases the flexibility of the heat transfer element 14 so that it is more readily able to navigate through blood vessels. The tube sections 25, 27 are also able to tolerate cryogenic temperatures without a loss of performance. The tube sections 25, 27 may have a predetermined thickness of their walls, such as between about 0.5 and 0.8 mils. The predetermined thickness is to a certain extent dependent on the diameter of the overall tube. Thicknesses of 0.5 to 0.8 mils may be appropriate especially for a tubal diameter of about 4 mm. For smaller diameters, such as about 3.3 mm, larger thicknesses may be employed for higher strength. In another embodiment, tube sections 25, 27 may be formed from a polymer material such as rubber, *e.g.*, latex rubber.

The exterior surfaces of the heat transfer element 14 can be made from metal except in flexible joint embodiments where the surface may be comprised of a polymer material. The metal may be a very high thermal conductivity material such as nickel, thereby facilitating efficient heat transfer. Alternatively, other metals such as stainless steel, titanium, aluminum, silver, copper and the like, can be used, with or without an appropriate coating or treatment to enhance biocompatibility or inhibit clot formation. Suitable biocompatible coatings include, *e.g.*, gold, platinum or polymer paralyene. The heat transfer element 14 may be manufactured by plating a thin layer of metal on a mandrel that has the appropriate pattern. In this way, the heat transfer element 14 may be manufactured inexpensively in large quantities, which is an important feature in a disposable medical device.

Because the heat transfer element 14 may dwell within the blood vessel for extended periods of time, such as 24-48 hours or even longer, it may be desirable to treat the surfaces of the heat transfer element 14 to avoid clot formation. One means by which to prevent thrombus formation is to bind an antithrombogenic agent to the surface of the heat transfer element 14. For example, heparin is known to inhibit clot formation and is also known to be useful as a biocoating. Alternatively, the surfaces of the heat transfer element 14 may be bombarded with ions such as nitrogen. Bombardment with nitrogen can harden and smooth the surface and, thus prevent adherence of clotting factors to the surface.

Figure 3 is a longitudinal sectional view of the heat transfer element 14, taken along line 3-3 in Figure 2. Some interior contours are omitted for purposes of clarity. An inner tube 42 creates an inner coaxial lumen 40 and an outer coaxial lumen 46 within the heat transfer element 14. Once the heat transfer element 14 is in place in the blood vessel, a working fluid such as saline or other aqueous solution may be circulated through the heat transfer element 14. Fluid flows up a supply catheter into the inner coaxial lumen 40. At the distal end of the heat transfer element 14, the working fluid exits the inner coaxial lumen 40 and enters the outer lumen 46. As the working fluid flows through the outer lumen 46, heat is transferred between the working fluid and the exterior surface 37 of the heat transfer element 14. Because the heat transfer element 14 is constructed from a high conductivity material, the temperature of its exterior surface 37 may reach very close to the temperature of the working fluid. The tube 42 may be formed as an insulating divider to thermally separate the inner lumen 40 from the outer lumen 46. For example, insulation may be achieved by creating longitudinal air channels in the wall of the insulating tube 42. Alternatively, the insulating tube 42 may be constructed of a non-thermally conductive material like polytetrafluoroethylene or some other polymer.

It is important to note that the same mechanisms that govern the heat transfer rate between the exterior surface 37 of the heat transfer element 14 and the blood also govern the heat transfer rate between the working fluid and the interior surface 38 of the heat transfer element 14. The heat transfer characteristics of the interior surface 38 are particularly important when using water, saline or other fluid which remains a liquid as the coolant. Other coolants such as freon undergo nucleate boiling and create turbulence through a different mechanism. Saline is a safe coolant because it is non-toxic, and leakage of saline does not result in a gas embolism, which could occur with the use of boiling refrigerants. Since turbulence in the coolant is enhanced by the shape of the interior surface 38 of the heat transfer element 14, the coolant can be delivered to the heat transfer element 14 at a warmer temperature and still achieve the necessary heat transfer rate.

This has a number of beneficial implications in the need for insulation along the catheter shaft length. Due to the decreased need for insulation, the catheter shaft diameter can be made smaller. The enhanced heat transfer characteristics of the interior surface of the heat transfer element 14 also allow the working fluid to be delivered to

the heat transfer element 14 at lower flow rates and lower pressures. High pressures may make the heat transfer element stiff and cause it to push against the wall of the blood vessel, thereby shielding part of the exterior surface 37 of the heat transfer element 14 from the blood. Because of the increased heat transfer characteristics
5 achieved by the alternating helical ridges 28, 32, 36, the pressure of the working fluid may be as low as 5 atmospheres, 3 atmospheres, 2 atmospheres or even less than 1 atmosphere.

Figure 4 is a transverse sectional view of the heat transfer element 14, taken at a location denoted by the line 4-4 in Figure 2. Figure 4 illustrates a five-lobed
10 embodiment, whereas Figure 2 illustrates a four-lobed embodiment. As mentioned earlier, any number of lobes might be used. In Figure 4, the coaxial construction of the heat transfer element 14 is clearly shown. The inner coaxial lumen 40 is defined by the insulating coaxial tube 42. The outer lumen 46 is defined by the exterior surface of the insulating coaxial tube 42 and the interior surface 38 of the heat transfer element 14. In
15 addition, the helical ridges 32 and helical grooves 30 may be seen in Figure 4. As noted above, in the preferred embodiment, the depth of the grooves, d_i , is greater than the boundary layer thickness which would have developed if a cylindrical heat transfer element were introduced. For example, in a heat transfer element 14 with a 4 mm outer diameter, the depth of the invaginations, d_i , may be approximately equal to 1 mm if
20 designed for use in the carotid artery. Although Figure 4 shows four ridges and four grooves, the number of ridges and grooves may vary. Thus, heat transfer elements with 1, 2, 3, 4, 5, 6, 7, 8 or more ridges are specifically contemplated.

Figure 5 is a perspective view of a heat transfer element 14 in use within a blood vessel, showing only one helical lobe per segment for purposes of clarity.
25 Beginning from the proximal end of the heat transfer element (not shown in Figure 5), as the blood moves forward during the systolic pulse, the first helical heat transfer segment 20 induces a counter-clockwise rotational inertia to the blood. As the blood reaches the second segment 22, the rotational direction of the inertia is reversed, causing turbulence within the blood. Further, as the blood reaches the third segment
30 24, the rotational direction of the inertia is again reversed. The sudden changes in flow direction actively reorient and randomize the velocity vectors, thus ensuring turbulence throughout the bloodstream. During turbulent flow, the velocity vectors of the blood become more random and, in some cases, become perpendicular to the axis of the

artery. In addition, as the velocity of the blood within the artery decreases and reverses direction during the cardiac cycle, additional turbulence is induced and turbulent motion is sustained throughout the duration of each pulse through the same mechanisms described above.

5 Thus, a large portion of the volume of warm blood in the vessel is actively brought in contact with the heat transfer element 14, where it can be cooled by direct contact rather than being cooled largely by conduction through adjacent laminar layers of blood. As noted above, the depth of the grooves 26, 30, 34 (Figure 2) is greater than the depth of the boundary layer that would develop if a straight-walled heat transfer
10 element were introduced into the blood stream. In this way, free stream turbulence is induced. In the preferred embodiment, in order to create the desired level of turbulence in the entire blood stream during the whole cardiac cycle, the heat transfer element 14 creates a turbulence intensity greater than about 0.05. The turbulence intensity may be greater than 0.05, 0.06, 0.07 or up to 0.10 or 0.20 or greater.

15 Referring back to Figure 2, the heat transfer element 14 has been designed to address all of the design criteria discussed above. First, the heat transfer element 14 is flexible and is made of a highly conductive material. The flexibility is provided by a segmental distribution of tube sections 25, 27 which provide an articulating mechanism. The tube sections have a predetermined thickness which provides
20 sufficient flexibility. Second, the exterior surface area 37 has been increased through the use of helical ridges 28, 32, 36 and helical grooves 26, 30, 34. The ridges also allow the heat transfer element 14 to maintain a relatively atraumatic profile, thereby minimizing the possibility of damage to the vessel wall. Third, the heat transfer element 14 has been designed to promote turbulent kinetic energy both internally and
25 externally. The modular or segmental design allows the direction of the invaginations to be reversed between segments. The alternating helical rotations create an alternating flow that results in a mixing of the blood in a manner analogous to the mixing action created by the rotor of a washing machine that switches directions back and forth. This mixing action is intended to promote high level turbulent kinetic energy to enhance the
30 heat transfer rate. The alternating helical design also causes beneficial mixing, or turbulent kinetic energy, of the working fluid flowing internally.

Figure 6 is a cut-away perspective view of an alternative embodiment of a heat transfer element 50. An external surface 52 of the heat transfer element 50 is covered

with a series of axially staggered protrusions 54. The staggered nature of the outer protrusions 54 is readily seen with reference to Figure 7 which is a transverse cross-sectional view taken at a location denoted by the line 7-7 in Figure 6. In order to induce free stream turbulence, the height, d_p , of the staggered outer protrusions 54 is greater than the thickness of the boundary layer which would develop if a smooth heat transfer element had been introduced into the blood stream. As the blood flows along the external surface 52, it collides with one of the staggered protrusions 54 and a turbulent wake flow is created behind the protrusion. As the blood divides and swirls along side of the first staggered protrusion 54, its turbulent wake encounters another staggered protrusion 54 within its path preventing the re-lamination of the flow and creating yet more turbulence. In this way, the velocity vectors are randomized and turbulence is created not only in the boundary layer but also throughout the free stream. As is the case with the preferred embodiment, this geometry also induces a turbulent effect on the internal coolant flow.

A working fluid is circulated up through an inner coaxial lumen 56 defined by an insulating coaxial tube 58 to a distal tip of the heat transfer element 50. The working fluid then traverses an outer coaxial lumen 60 in order to transfer heat to the exterior surface 52 of the heat transfer element 50. The inside surface of the heat transfer element 50 is similar to the exterior surface 52, in order to induce turbulent flow of the working fluid. The inner protrusions can be aligned with the outer protrusions 54, as shown in Figure 7, or they can be offset from the outer protrusions 54, as shown in Figure 6.

Figure 8 is a schematic representation of the invention being used to cool the brain of a patient. The selective organ hypothermia apparatus shown in Figure 8 includes a working fluid supply 10, preferably supplying a chilled liquid such as water, alcohol or a halogenated hydrocarbon, a supply catheter 12 and the heat transfer element 14. The supply catheter 12 has a coaxial construction. An inner coaxial lumen within the supply catheter 12 receives coolant from the working fluid supply 10. The coolant travels the length of the supply catheter 12 to the heat transfer element 14 which serves as the cooling tip of the catheter. At the distal end of the heat transfer element 14, the coolant exits the insulated interior lumen and traverses the length of the heat transfer element 14 in order to decrease the temperature of the heat transfer element 14. The coolant then traverses an outer lumen of the supply catheter 12 so that

it may be disposed of or recirculated. The supply catheter 12 is a flexible catheter having a diameter sufficiently small to allow its distal end to be inserted percutaneously into an accessible artery such as the femoral artery of a patient as shown in Figure 8. The supply catheter 12 is sufficiently long to allow the heat transfer element 14 at the distal end of the supply catheter 12 to be passed through the vascular system of the patient and placed in the internal carotid artery or other small artery. The method of inserting the catheter into the patient and routing the heat transfer element 14 into a selected artery is well known in the art.

Although the working fluid supply 10 is shown as an exemplary cooling device, other devices and working fluids may be used. For example, in order to provide cooling, freon, perfluorocarbon, water, or saline may be used, as well as other such coolants.

The heat transfer element can absorb or provide over 75 Watts of heat to the blood stream and may absorb or provide as much as 100 Watts, 150 Watts, 170 Watts or more. For example, a heat transfer element with a diameter of 4 mm and a length of approximately 10 cm using ordinary saline solution chilled so that the surface temperature of the heat transfer element is approximately 5°C and pressurized at 2 atmospheres can absorb about 100 Watts of energy from the bloodstream. Smaller geometry heat transfer elements may be developed for use with smaller organs which provide 60 Watts, 50 Watts, 25 Watts or less of heat transfer.

The practice of the present invention is illustrated in the following non-limiting example.

Exemplary Procedure

1. The patient is initially assessed, resuscitated, and stabilized.
2. The procedure is carried out in an angiography suite or surgical suite equipped with fluoroscopy.
3. Because the catheter is placed into the common carotid artery, it is important to determine the presence of stenotic atheromatous lesions. A carotid duplex (Doppler/ultrasound) scan can quickly and non-invasively make this determination.
- The ideal location for placement of the catheter is in the left carotid so this may be scanned first. If disease is present, then the right carotid artery can be assessed. This test can be used to detect the presence of proximal common carotid lesions by observing the slope of the systolic upstroke and the shape of the pulsation. Although

these lesions are rare, they could inhibit the placement of the catheter. Examination of the peak blood flow velocities in the internal carotid can determine the presence of internal carotid artery lesions. Although the catheter is placed proximally to such lesions, the catheter may exacerbate the compromised blood flow created by these lesions. Peak systolic velocities greater than 130 cm/sec and peak diastolic velocities > 100 cm/sec in the internal indicate the presence of at least 70% stenosis. Stenosis of 70% or more may warrant the placement of a stent to open up the internal artery diameter.

4. The ultrasound can also be used to determine the vessel diameter and the blood flow and the catheter with the appropriately sized heat transfer element could be selected.

5. After assessment of the arteries, the patients inguinal region is sterilely prepped and infiltrated with lidocaine.

6. The femoral artery is cannulated and a guide wire may be inserted to the desired carotid artery. Placement of the guide wire is confirmed with fluoroscopy.

7. An angiographic catheter can be fed over the wire and contrast media injected into the artery to further to assess the anatomy of the carotid.

8. Alternatively, the femoral artery is cannulated and a 10-12.5 french (f) introducer sheath is placed.

9. A guide catheter is placed into the desired common carotid artery. If a guiding catheter is placed, it can be used to deliver contrast media directly to further assess carotid anatomy.

10. A 10 f -12 f (3.3- 4.0 mm) (approximate) cooling catheter is subsequently filled with saline and all air bubbles are removed.

11. The cooling catheter is placed into the carotid artery via the guiding catheter or over the guidewire. Placement is confirmed with fluoroscopy.

12. Alternatively, the cooling catheter tip is shaped (angled or curved approximately 45 degrees), and the cooling catheter shaft has sufficient pushability and torqueability to be placed in the carotid without the aid of a guide wire or guide catheter.

13. The cooling catheter is connected to a pump circuit also filled with saline and free from air bubbles. The pump circuit has a heat exchange section that is immersed into a water bath and tubing that is connected to a peristaltic pump. The water bath is chilled to approximately 0°C.

14. Cooling is initiated by starting the pump mechanism. The saline within the cooling catheter is circulated at 5 cc/sec. The saline travels through the heat exchanger in the chilled water bath and is cooled to approximately 1°C.
15. The saline subsequently enters the cooling catheter where it is delivered to the heat transfer element. The saline is warmed to approximately 5-7°C as it travels along the inner lumen of the catheter shaft to the end of the heat transfer element.
16. The saline then flows back through the heat transfer element in contact with the inner metallic surface. The saline is further warmed in the heat transfer element to 12-15°C, and in the process, heat is absorbed from the blood, cooling the blood to 30°C to 32°C.
17. The chilled blood then goes on to chill the brain. It is estimated that 15-30 minutes will be required to cool the brain to 30 to 32°C.
18. The warmed saline travels back down the outer lumen of the catheter shaft and back to the chilled water bath where it is cooled to 1°C.
19. The pressure drops along the length of the circuit are estimated to be 2-3 atmospheres.
20. The cooling can be adjusted by increasing or decreasing the flow rate of the saline. Monitoring of the temperature drop of the saline along the heat transfer element will allow the flow to be adjusted to maintain the desired cooling effect.
21. The catheter is left in place to provide cooling for 12 to 24 hours.
22. If desired, warm saline can be circulated to promote warming of the brain at the end of the procedure.

The invention may also be used in combination with other techniques. For example, one technique employed to place working lumens or catheters in desired locations employs guide catheters, as mentioned above. Referring to Figure 9, a guide catheter 102 is shown which may be advantageously employed in the invention. The guide catheter 102 has a soft tapered tip 104 and a retaining flange 124 at a distal end 101. The soft tapered tip 104 allows an atraumatic entrance of the guide catheter 102 into an artery as well as a sealing function as is described in more detail below. The retaining flange 124 may be a metallic member adhered to the guide catheter interior

wall or may be integral with the material of the tube. The retaining flange 124 further has a sealing function described in more detail below.

The guide catheter 102 may have various shapes to facilitate placement into particular arteries. In the case of the carotid artery, the guide catheter 102 may have the shape of a hockey stick. The guide catheter 102 may include a Pebax® tube with a Teflon® liner. The Teflon® liner provides sufficient lubricity to allow minimum friction when components are pushed through the tube. A metal wire braid may also be employed between the Pebax® tube and the Teflon® liner to provide torqueability of the guide catheter 102.

10 A number of procedures may be performed with the guide catheter 102 in place within an artery. For example, a stent may be disposed across a stenotic lesion in the internal carotid artery. This procedure involves placing a guide wire through the guide catheter 102 and across the lesion. A balloon catheter loaded with a stent is then advanced along the guide wire. The stent is positioned across the lesion. The balloon
15 is expanded with contrast, and the stent is deployed intravascularly to open up the stenotic lesion. The balloon catheter and the guide wire may then be removed from the guide catheter.

A variety of treatments may pass through the guide catheter. For example, the guide catheter, or an appropriate lumen disposed within, may be employed to transfer
20 contrast for diagnosis of bleeding or arterial blockage, such as for angiography. The same may further be employed to deliver various drug therapies, *e.g.*, to the brain. Such therapies may include delivery of thrombolytic drugs that lyse clots lodged in the arteries of the brain.

A proximal end 103 of the guide catheter 102 has a male luer connector for
25 mating with a y-connector 118 attached to a supply tube 108. The supply tube 108 may include a braided Pebax® tube or a polyimide tube. The y-connector 118 connects to the guide catheter 102 via a male/female luer connector assembly 116. The y-connector 118 allows the supply tube 108 to enter the assembly and to pass through the male/female luer connector assembly 116 into the interior of the guide catheter 102.
30 The supply tube 108 may be disposed with an outlet at its distal end. The outlet of the supply tube 108 may also be used to provide a working fluid to the interior of a heat transfer element 110. The guide catheter 102 may be employed as the return tube for the working fluid supply in this aspect of the invention. In this embodiment, a heat

transfer element 110 is delivered to the distal end 101 of the guide catheter 102 as is shown in Figure 10.

In Figure 10, the heat transfer element 110 is shown, nearly in a working location, in combination with the return tube / guide catheter 102. In particular, the heat transfer element 110 is shown near the distal end 101 of the return tube / guide catheter ("RTGC") 102. The heat transfer element 110 may be kept in place by a flange 106 on the heat transfer element 110 that abuts the retaining flange 124 on the RTGC 102. Flanges 124 and 106 may also employ o-rings such as an o-ring 107 shown adjacent to the flange 106. Other such sealing mechanisms or designs may also be used. In this way, the working fluid is prevented from leaking into the blood.

The supply tube 108 may connect to the heat transfer element 110 (the connection is not shown) and may be employed to push the heat transfer element 110 through the guide catheter 102. The supply tube should have sufficient rigidity to accomplish this function. In an alternative embodiment, a guide wire may be employed having sufficient rigidity to push both the supply tube 108 and the heat transfer element 110 through the guide catheter 102. So that the supply tube 108 is preventing from abutting its outlet against the interior of the heat transfer element 110 and thereby stopping the flow of working fluid, a strut 112 may be employed on a distal end of the supply tube 108. The strut 112 may have a window providing an alternative path for the flowing working fluid.

The heat transfer element 110 may employ any of the forms disclosed above, as well as variations of those forms. For example, the heat transfer element 110 may employ alternating helical ridges separated by flexible joints, the ridges creating sufficient turbulence to enhance heat transfer between a working fluid and blood in the artery. Alternatively, the heat transfer element 110 may be inflatable and may have sufficient surface area that the heat transfer due to conduction alone is sufficient to provide the requisite heat transfer. Details of the heat transfer element 110 are omitted in Figure 10 for clarity.

Figure 11 shows an alternate embodiment of the invention in which a heat transfer element 204 employs an internal supply catheter 216. The heat transfer element 204 is shown with turbulence-inducing invaginations 218 located thereon. Similar invaginations may be located in the interior of the heat transfer element 204 but are not shown for clarity. Further, it should be noted that the heat transfer element 204

is shown with merely four invaginations. Other embodiments may employ multiple elements connected by flexible joints as is disclosed above. A single heat transfer element is shown in Figure 11 merely for clarity.

A return supply catheter 202 is shown coupled to the heat transfer element 204.

- 5 The return supply catheter may be coupled to the heat transfer element 204 in known fashion, and may provide a convenient return path for working fluid as may be provided to the heat transfer element 204 to provide temperature control of a flow or volume of blood.

- 10 A delivery catheter 216 is also shown in Figure 11. The delivery catheter 216 may be coupled to a y-connector at its proximal end in the manner disclosed above. The delivery catheter 216 may be freely disposed within the interior of the return supply catheter 202 except where it is restrained from further longitudinal movement (in one direction) by a retaining flange 210 disposed at the distal end 208 of the heat transfer element 204. The delivery catheter 216 may be made sufficiently flexible to
15 secure itself within retaining flange 210, at least for a short duration. The delivery catheter 216 may have a delivery outlet 212 at a distal end to allow delivery of a drug or other such material for therapeutic purposes. For example, a radioopaque fluid may be dispensed for angiography or a thrombolytic drug for thrombolysis applications.

- For applications in which it is desired to provide drainage of the artery, *e.g.*,
20 laser ablation, the delivery catheter may be pulled upstream of the retaining flange 210, exposing an annular hole in fluid communication with the return supply catheter 202. The return supply catheter 202 may then be used to drain the volume adjacent the retaining flange 210.

- The assembly may also perform temperature control of blood in the artery
25 where the same is located. Such temperature control procedures may be performed, *e.g.*, before or after procedures involving the delivery catheter 216. Such a device for temperature control is shown in Figure 12. In this figure, a working fluid catheter 222 is disposed within the return supply catheter 202 and the heat transfer element 204. In a manner similar to the delivery catheter 216, the working fluid catheter may be freely
30 disposed within the interior of the return supply catheter 202 and may further be coupled to a y-connector at its proximal end in the manner disclosed above. The working fluid catheter 222 may further be made sufficiently flexible to secure itself within retaining flange 210, at least for a short duration. The working fluid catheter

222 may have a plurality of outlets 214 to allow delivery of a working fluid. The outlets 214 are located near the distal end 224 of the working fluid catheter 222 but somewhat upstream. In this way, the outlets 214 allow dispensation of a working fluid into the interior of the heat transfer element 204 rather than into the blood stream. The
5 working fluid catheter 222 may also be insulated to allow the working fluid to maintain a desired temperature without undue heat losses to the walls of the working fluid catheter 222.

One way of using the same catheter as a delivery catheter and as a working fluid catheter is shown in Figures 14 and 15. In Figure 14, a delivery/working fluid catheter
10 248 is shown in a position similar to the respective catheters of Figures 11 and 12. The delivery/working fluid catheter 248 has working fluid outlets and a delivery outlet, and is further equipped with a balloon 244 disposed at the distal end. Balloon 244 may be inflated with a separate lumen (not shown). By retracting the delivery/working fluid catheter 248 to the position shown in Figure 15, the balloon 244 may be made to seal
15 the hole defined by retaining flange 210, thereby creating a fluid-tight seal so that working fluid may be dispensed from outlets 246 to heat or cool the heat transfer element 204.

One method of disposing a heat transfer device within a desired artery, such as the carotid artery, involves use of a guide wire. Referring to Figure 13, a guide wire
20 232 is shown disposed within the interior of the heat transfer element 204. The heat transfer element 204 may conveniently use the hole defined by retaining flange 210 to be threaded onto the guide wire 232.

Numerous other therapies may then employ the return supply catheter and heat transfer element as a "guide catheter". For example, various laser and ultrasound
25 ablation catheters may be disposed within. In this way, these therapeutic techniques may be employed at nearly the same time as therapeutic temperature control, including, *e.g.*, neuroprotective cooling.

The use of an additional lumen was disclosed above in connection with passing a variety of treatments through the guide catheter. For example, an additional lumen
30 may be employed to transfer contrast for diagnosis of bleeding or arterial blockage, such as for angiography. Such an additional lumen may be defined by a drug delivery catheter which forms a part of the overall catheter assembly. The same may be employed to deliver various drug therapies, *e.g.*, to the brain. The use of an additional

lumen was further mentioned in connection with expansion of a balloon that may be used to occlude a drug delivery lumen outlet.

Figure 16 depicts an implementation of an embodiment of the invention employing just such a third lumen. In Figure 16, a third lumen 316 is a small central
5 lumen defined by a drug delivery catheter substantially coaxial with the supply and return catheters. A return catheter 302 defining an outlet lumen 320 is coupled to a heat transfer element 304 as before. The heat transfer element 304 may have turbulence-inducing invaginations 306 thereon. Within the heat transfer element 304 and the return catheter 302 is an inlet lumen 318 defined by a supply catheter 310. The
10 inlet lumen 318 may be used to deliver a working fluid to the interior of the heat transfer element 304. The outlet lumen 320 may be used to return or exhaust the working fluid from the heat transfer element 304. As above, their respective functions may also be reversed. The radius of the return catheter may be greater or less than the radius of the supply catheter. The working fluid may be used to heat or cool the heat
15 transfer element which in turn heats or cools the fluid surrounding the heat transfer element.

A drug delivery catheter 312 defines the third lumen 316 and as shown may be coaxial with the inlet lumen 318 and the outlet lumen 320. Of course, the delivery catheter 312 may be also be off-axis or non-coaxial with respect to the inlet lumen 318
20 and the outlet lumen 320.

For example, as shown in Figure 17, the drug delivery catheter may be a lumen 316' within the return catheter and may be further defined by a catheter wall 312'. As another example, as shown in Figure 18, the drug delivery catheter may be a lumen 316'' adjacent to and parallel to the return catheter and may be further defined by a
25 catheter wall 312''. In an alternative embodiment, more than one lumen may be provided within the return catheter to allow delivery of several types of products, *e.g.*, thrombolytics, saline solutions, etc. Of course, the supply catheter may also be used to define the drug delivery catheter. The drug delivery catheter may be substantial coaxial with respect to the return catheter or supply catheter or both, or may alternatively be
30 off-axis. The drug delivery catheter includes an outlet at a distal end thereof. The outlet may be distal or proximal of the distal end of the return or supply catheters. The outlet may be directed parallel to the return or supply catheters or may alternatively be directed transverse of the return or supply catheters.

The device may be inserted in a selected feeding vessel in the vascular system of a patient. For example, the device may be inserted in an artery which feeds a downstream organ or which feeds an artery which, in turn, feeds a downstream organ. In any of the embodiments of Figures 16-18, the drug delivery catheter lumen may be used to deliver a drug, liquid, or other material to the approximate location of the heat transfer element. Such delivery may occur before, after, or contemporaneous with heat transfer to or from the blood. In this way, drugs or enzymes which operate at temperatures other than normal body temperature may be used by first altering the local blood temperature with the heat transfer element and then delivering the temperature specific drug, such as a temperature specific thrombolytic, which then operates at the altered temperature. Alternatively, such "third" lumens (with the supply and return catheters for the working fluid defining "first" and "second" lumens) may be used to remove particles, debris, or other desired products from the blood stream.

Figures 19 and 20 show another embodiment of the invention that is related to the embodiment of Figure 17. In this embodiment, several additional sealed lumens are disposed in the return catheter. Some of the lumens may be for drug delivery and others may be used to enhance turbulence in a manner described below. The sealed lumens are in pressure communication with a supply of air to inflate the same. In Figure 19, a return catheter 302' has one lumen 316'''C as shown for drug delivery. Another, lumen 316'''I, is shown which may be employed to alter the geometry and shape of the overall catheter. That is, inflating lumen 316'''I causes the lumen to expand in the same way that inflating a balloon causes it to expand. In order to allow for the expansion, appropriately reduced return catheter wall thicknesses may be employed. Also, inflatable lumens 316'''A-B and 316'''D-N may be distributed in a substantially symmetric fashion around the circumference of the catheter for a uniform inflation if desired. Of course, less distortion under inflation may occur at or adjacent lumens such as 316'''C used for drug delivery, as these do not inflate.

The inflatable lumens 316'''A-B and 316'''D-N may be caused to inflate under influence of, e.g., an air compressor with a variable air delivery flow. Rapid pulses of air may be used to inflate the lumens 316'''A-B and 316'''D-N in a rapid and repeated fashion. By so doing, the outer walls defining these lumens move rapidly into and out of the bloodstream around the catheter, inducing turbulence. Preferably, the amplitude of the vibrations is large enough to move the outer walls defining the lumens out of the

boundary layer and into the free stream of blood. This effect produces turbulence which is used to enhance heat transfer. As it is important to induce turbulence only near the heat transfer element, the area of appropriate wall thickness to allow for inflation need only be at, near, or adjacent the portion of the return catheter exterior wall adjacent the heat transfer element. In other words, the return catheter wall only requires reduction near the heat transfer element. The remainder of the catheter wall may remain thick for strength and durability.

The supply catheter 310 may be constructed such that the same does not contact the interior of the distal end 308 of the heat transfer element, which may cause a subsequent stoppage of flow of the working fluid. Such construction may be via struts located in the return catheter 302 that extend radially inwards and secure the supply catheter 310 from longitudinal translations. Alternatively, struts may extend longitudinally from the distal end of the supply catheter 310 and hold the same from contacting the heat transfer element. This construction is similar to strut 112 shown in Figure 10.

Figure 21 shows an alternate method of accomplishing this goal. In Figure 21, a heat transfer element 304' has an orifice 326 at a distal end 308. A supply catheter 310' is equipped with a drug delivery catheter 312' extending coaxially therein. The drug delivery catheter 312 may be formed of a solid material integral with supply catheter 310', or the two may be bonded after being constructed of separate pieces, or the two may remain separate during use, with a friction fit maintaining their positions with respect to each other. The supply catheter 310' is "in position" when a tapered portion 324 of the same is lodged in the hole 326 in the heat transfer element 304'. The tapered portion 324 should be lodged tightly enough to cause a strong friction fit so that working fluid does not leak through the hole 326. However, the tapered portion 324 should be lodged loosely enough to allow the supply catheter 310' to be removed from the heat transfer element 304' if continued independent use of the return catheter is desired.

The supply catheter 310' has a plurality of outlets 322. Outlets 322 are provided at points generally near or adjacent the distal end of the supply catheter 310'. The outlets are provided such that, when the supply catheter 310' is in position, the outlets generally face the heat transfer element 304'. In this way, the working fluid, emerging from the outlets 322, more directly impinges on the interior wall of the heat

transfer element 304'. In particular, the working fluid exits the interior of the supply catheter and flows into a volume defined by the exterior of the supply catheter and the interior of the heat transfer element.

For clarity, Figure 21 does not show the invaginations on the interior wall of the heat transfer element 304'. However, it will be understood that such invaginations may be present and may allow for enhanced heat transfer in combination with the emerging working fluid.

In the embodiments of Figures 9, 11, and 13-21, various types of catheter assemblies employing drug delivery catheters are described. In those embodiments, and particularly in the embodiments such as Figures 11, 14-16 and 21, in which a distal end of the drug delivery catheter protrudes substantially from the distal end of the remainder of the catheter assembly, a therapy may be performed in which the distal end of the catheter is embedded into a clot to be dissolved. An enzyme solution, such as a warm or cool enzyme solution, may then be sent directly into the clot to locally enhance the fibrinolytic activity.

In particular, the catheter may be placed as described above. In this procedure, however, the catheter is placed such that the tip of the protruding drug delivery catheter touches, is substantially near, or becomes embedded within the clot. An enzyme solution or other such drug is then delivered down the drug delivery catheter directly into the clot or into the volume of blood surrounding the clot. The enzyme solution may include tPA, streptokinase, urokinase, pro-urokinase, combinations thereof, and may be heated to enhance fibrinolytic activity. In a related embodiment, the solution may be a simple heated saline solution. The heated saline solution warms the clot, or the volume surrounding the clot, again leading to enhanced fibrinolytic activity.

In these procedures, it is advantageous to use embodiments of the invention in which the distal tip of the drug delivery catheter is substantially protruding, or is distal, from the remainder of the catheter assembly. In this way, the distal tip may be disposed adjacent to or within a clot without being obstructed by the remainder of the catheter assembly.

The invention has been described with respect to certain embodiments. It will be clear to one of skill in the art that variations of the embodiments may be employed in the method of the invention. Accordingly, the invention is limited only by the scope of the appended claims.

What Is Claimed Is:**CLAIMS**

1. A device for heating or cooling a surrounding fluid in a feeding vessel,
5 comprising:
a catheter assembly capable of insertion to a selected feeding vessel in the
vascular system of a patient, including:
a heat transfer element at a distal end of the catheter assembly, the heat
transfer element having a plurality of exterior surface irregularities shaped and
10 arranged to create turbulence in a surrounding fluid;
a supply catheter to deliver a working fluid to an interior of the heat
transfer element;
a return catheter to return a working fluid from the interior of the heat
transfer element; and
15 a drug delivery catheter running substantially parallel to the axis of the
catheter assembly.
2. The device of claim 1, wherein the drug delivery catheter is disposed
substantially coaxially with respect to the supply catheter.
- 20 3. The device of claim 2, wherein the drug delivery catheter includes an
outlet at a distal end thereof, the distal end of the drug delivery catheter distal of
a distal end of the return or supply catheters.
- 25 4. The device of claim 1, wherein the drug delivery catheter is disposed
within one of the return catheter or the supply catheter or both.
5. The device of claim 4, wherein the drug delivery catheter includes an
outlet transverse to the axis of the catheter assembly.
- 30 6. The device of claim 1, wherein:
the surface irregularities comprise a helical ridge and a helical groove
formed on each of successive heat transfer segments; and

the helical ridge on each heat transfer segment has an opposite helical twist to the helical ridges on adjacent heat transfer segments.

5 7. The device of claim 1, further comprising at least one sealed lumen within one of the return catheter or the supply catheter or both, the sealed lumen in pressure communication with a supply of air to inflate the sealed lumen.

10 8. The device of claim 1, wherein the return catheter is coaxial with the supply catheter, and the return catheter has a larger radius than the supply catheter.

15 9. The device of claim 1, wherein the return catheter is coaxial with the supply catheter, and the return catheter has a smaller radius than the supply catheter.

10. A device for heating or cooling a surrounding fluid in a feeding vessel, comprising:

a catheter assembly capable of insertion to a selected feeding vessel in the vascular system of a patient, including:

20 a heat transfer element at a distal end of the catheter assembly, the heat transfer element having a plurality of exterior surface irregularities shaped and arranged to create turbulence in a surrounding fluid, a distal end of the heat transfer element defining an orifice;

25 a supply catheter to deliver a working fluid to an interior of the heat transfer element, the supply catheter having a working fluid catheter disposed therein and further having disposed therein a drug delivery catheter running substantially parallel to the axis of the supply catheter, the working fluid catheter having defined thereon a number of outlets to communicate the working fluid from the interior of the supply catheter to a volume defined by the exterior of the supply catheter and the interior of the heat transfer element; and

30 a return catheter to return the working fluid from the interior of the heat transfer element.

11. A device for heating or cooling a surrounding fluid in a feeding vessel, comprising:

a catheter assembly capable of insertion to a selected feeding vessel in the vascular system of a patient, including:

5 a guide catheter capable of insertion to a selected feeding artery in the vascular system of a patient, the guide catheter having a soft tip and an interior retaining flange at a distal end;

a flexible supply tube capable of insertion in the guide catheter;

10 a heat transfer element attached to a distal end of the supply tube, the heat transfer element having a flange at a distal end, the flange capable of engagement with the retaining flange to prevent the heat transfer element from disengaging with the guide catheter; and

15 a plurality of exterior surface irregularities on the heat transfer element, the surface irregularities being shaped and arranged to create turbulence in surrounding fluid.

12. The device of claim 11, further comprising a strut coupled to the supply tube at a distal end thereof.

20 13. The device of claim 11, wherein the heat transfer element comprises a plurality of heat transfer segments, and further comprising a flexible joint connecting each of the heat transfer segments to adjacent the heat transfer segments.

25 14. The device of claim 13, wherein the flexible joint comprises a joint selected from the group consisting of a bellows, a metal tube, a plastic tube, a rubber tube, and a latex rubber tube.

30 15. The device of claim 11, wherein:
the surface irregularities comprise a helical ridge and a helical groove formed on each the heat transfer segment; and
the helical ridge on each the heat transfer segment has an opposite helical twist to the helical ridges on adjacent the heat transfer segments.

1/13

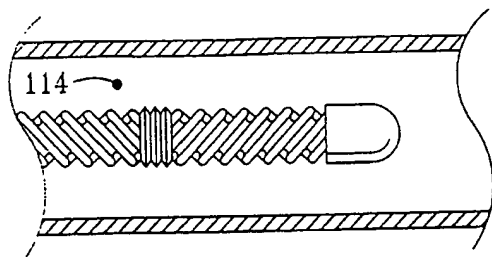


Fig. 1

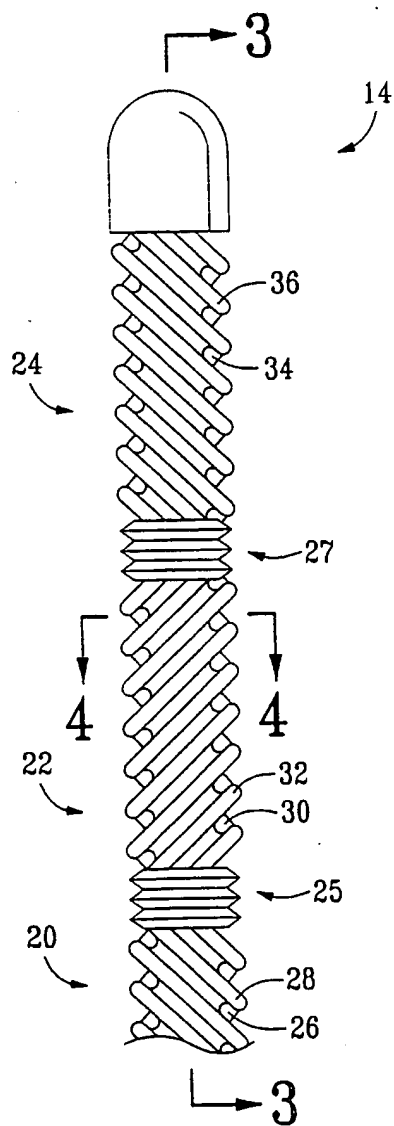


Fig. 2

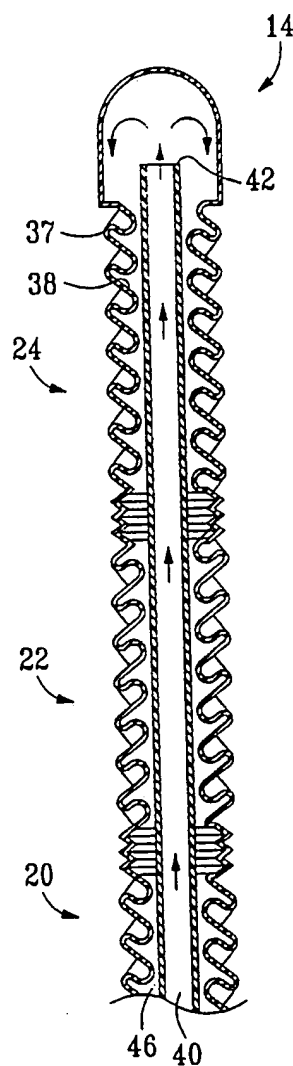


Fig. 3

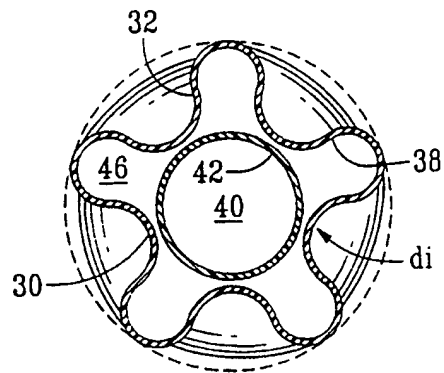


FIG. 4

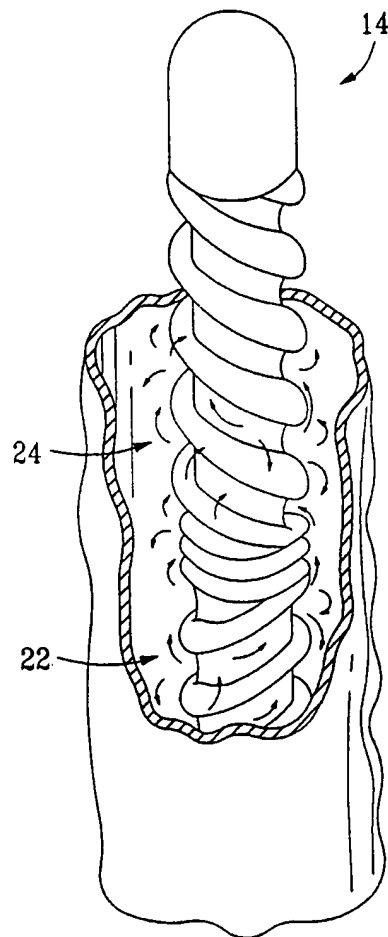


FIG. 5

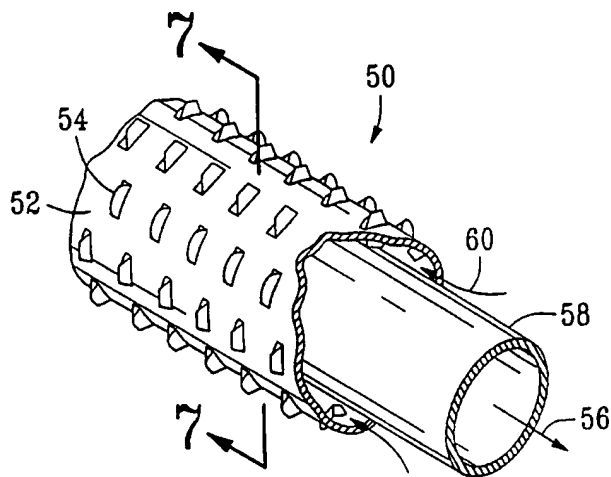
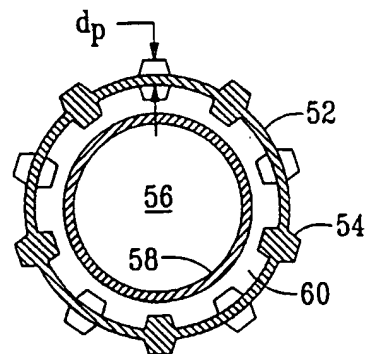
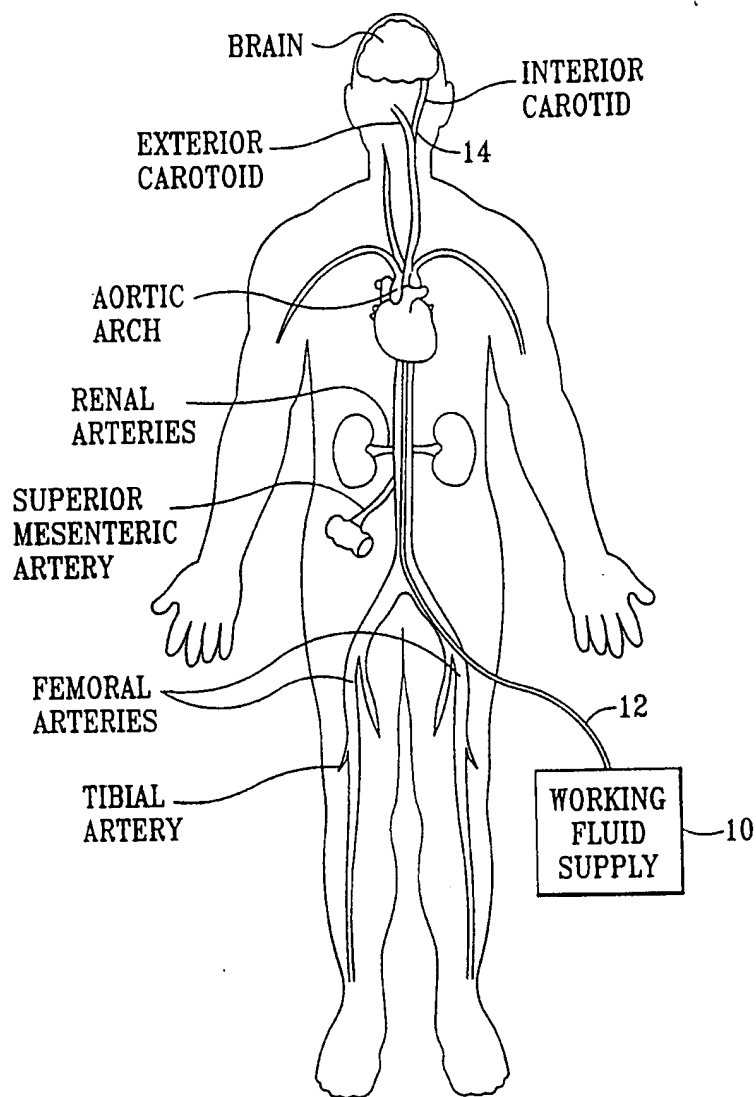


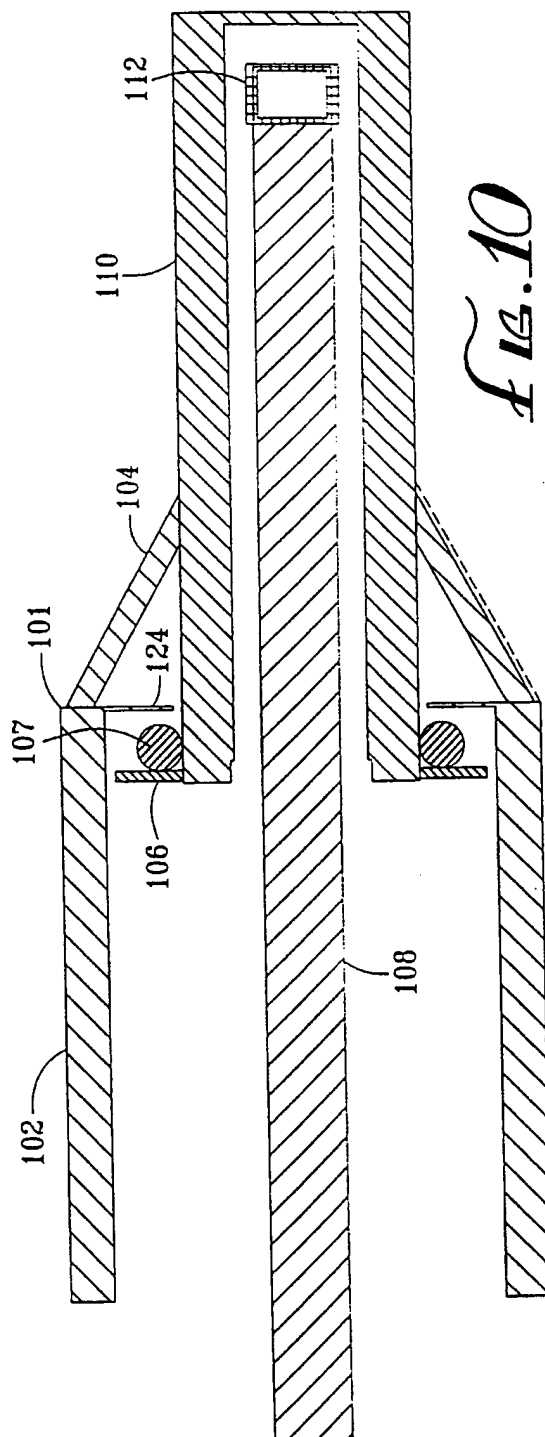
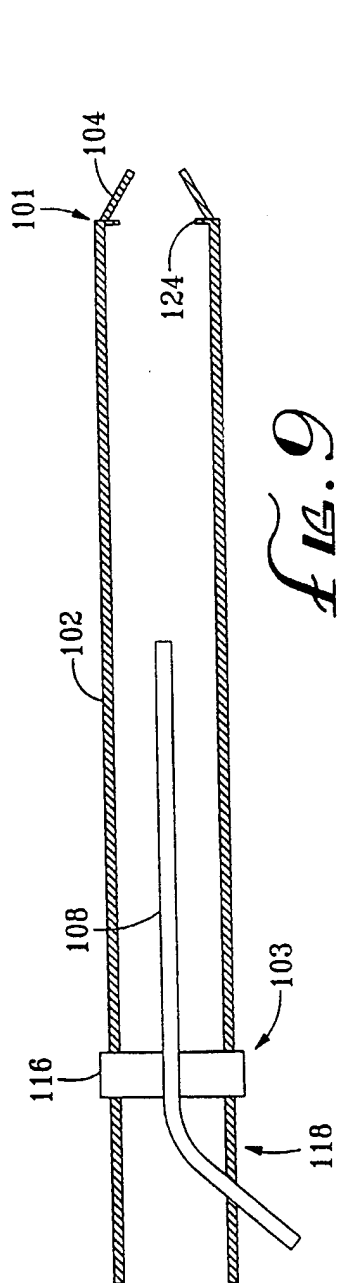
FIG. 6

FIG. 7



3/13

*Fig. 8*



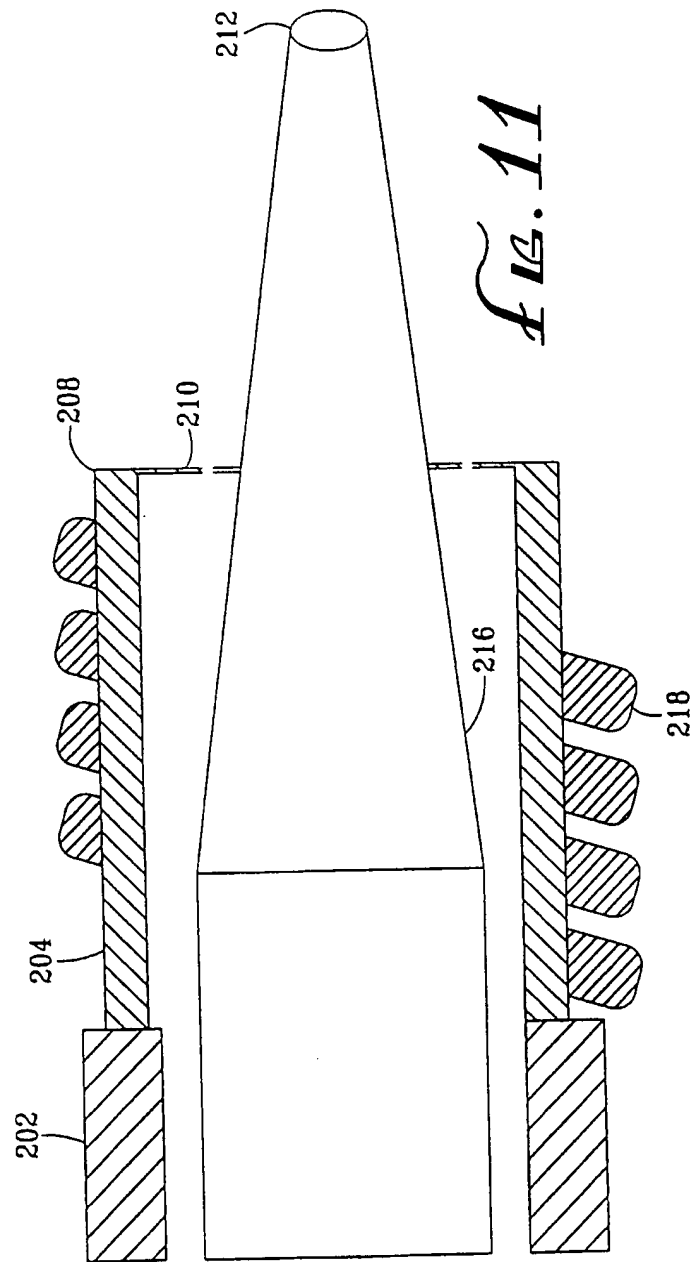
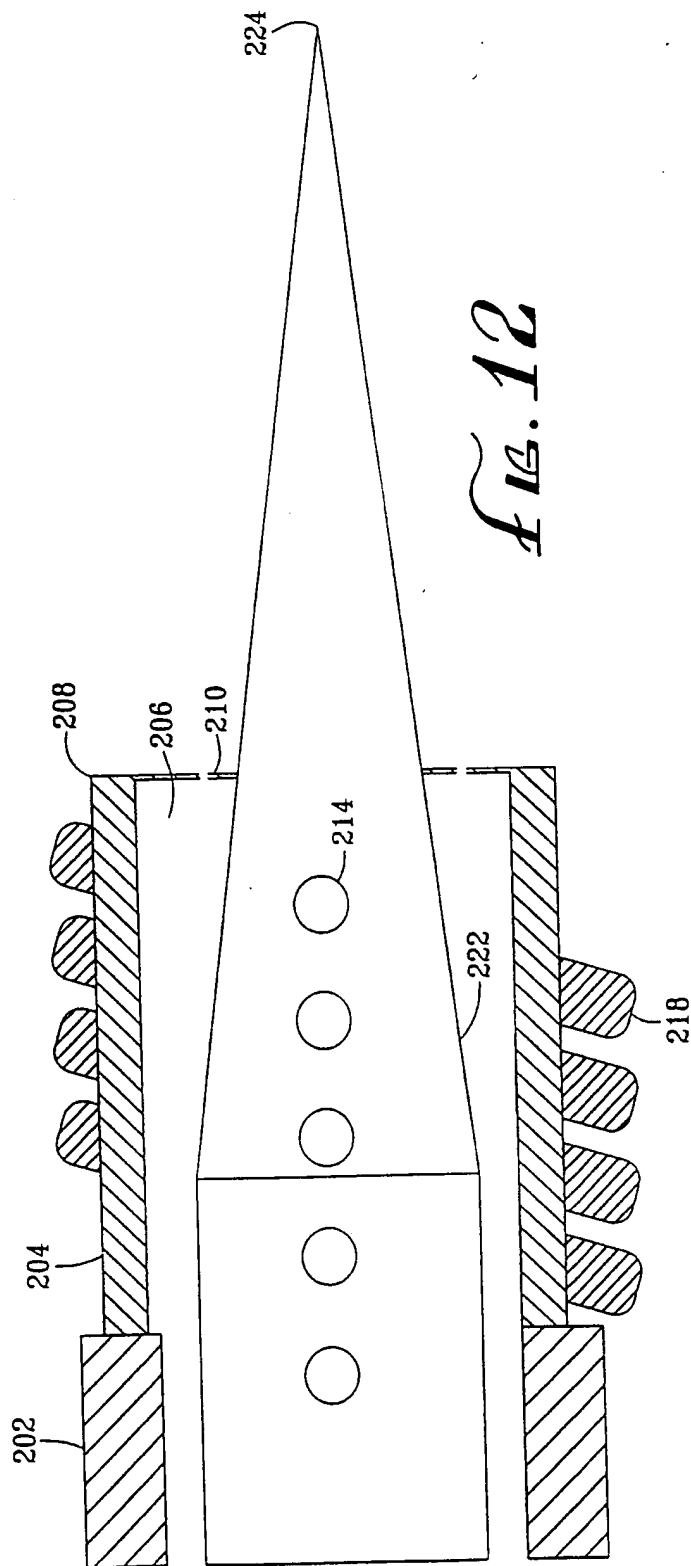


FIG. 11

6/13



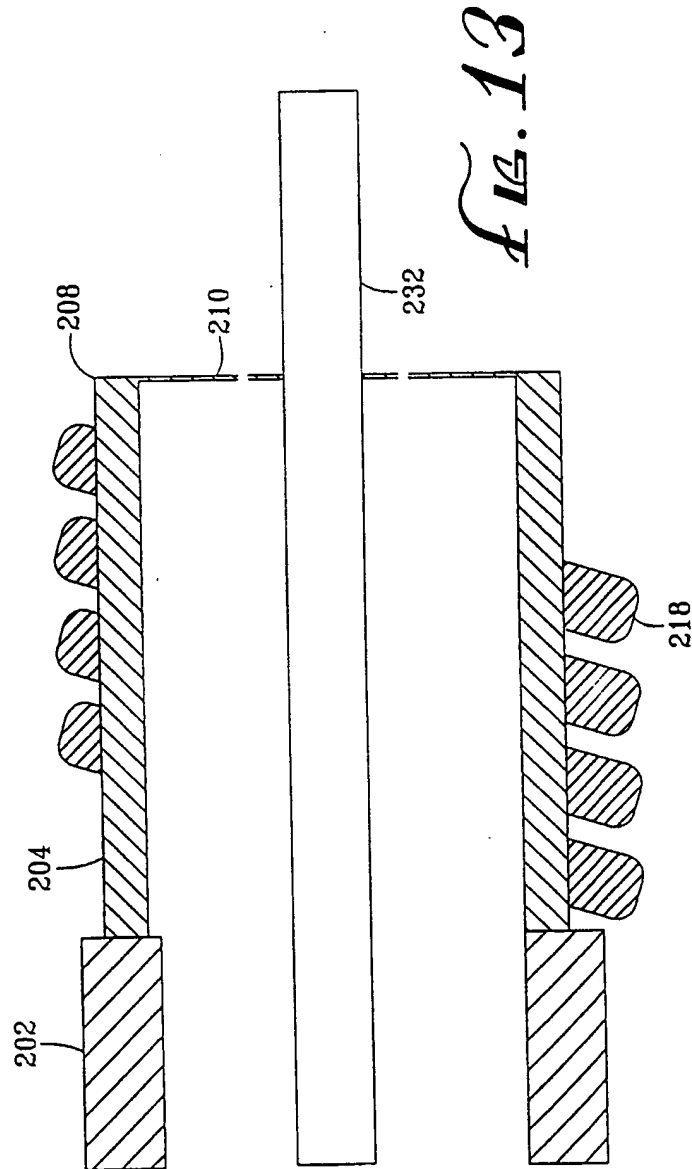


Fig. 13

8/13

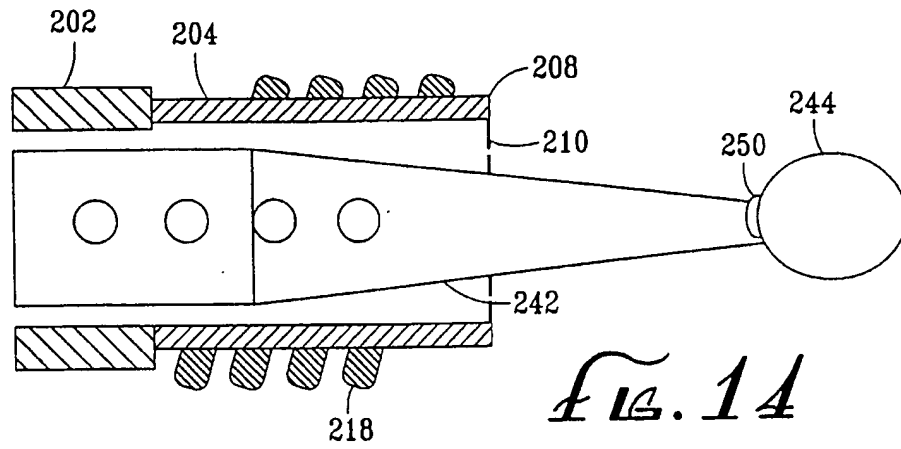


Fig. 14

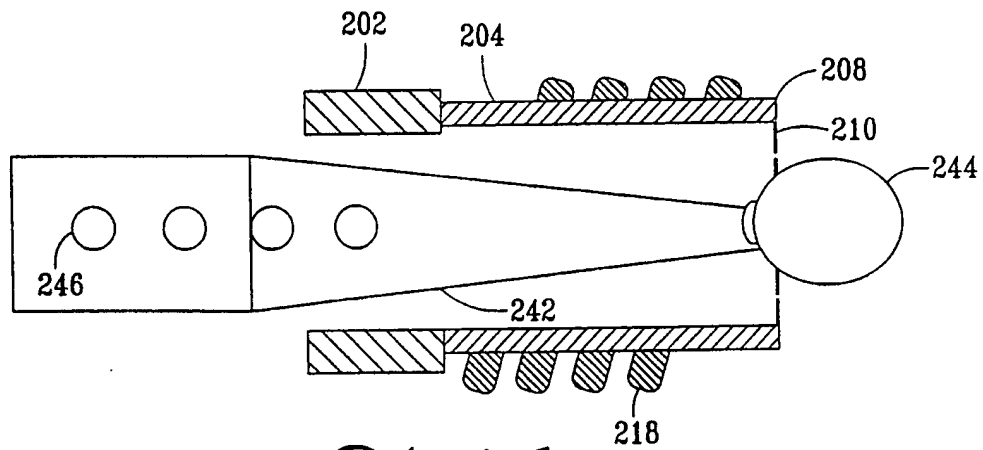


Fig. 15

9/13

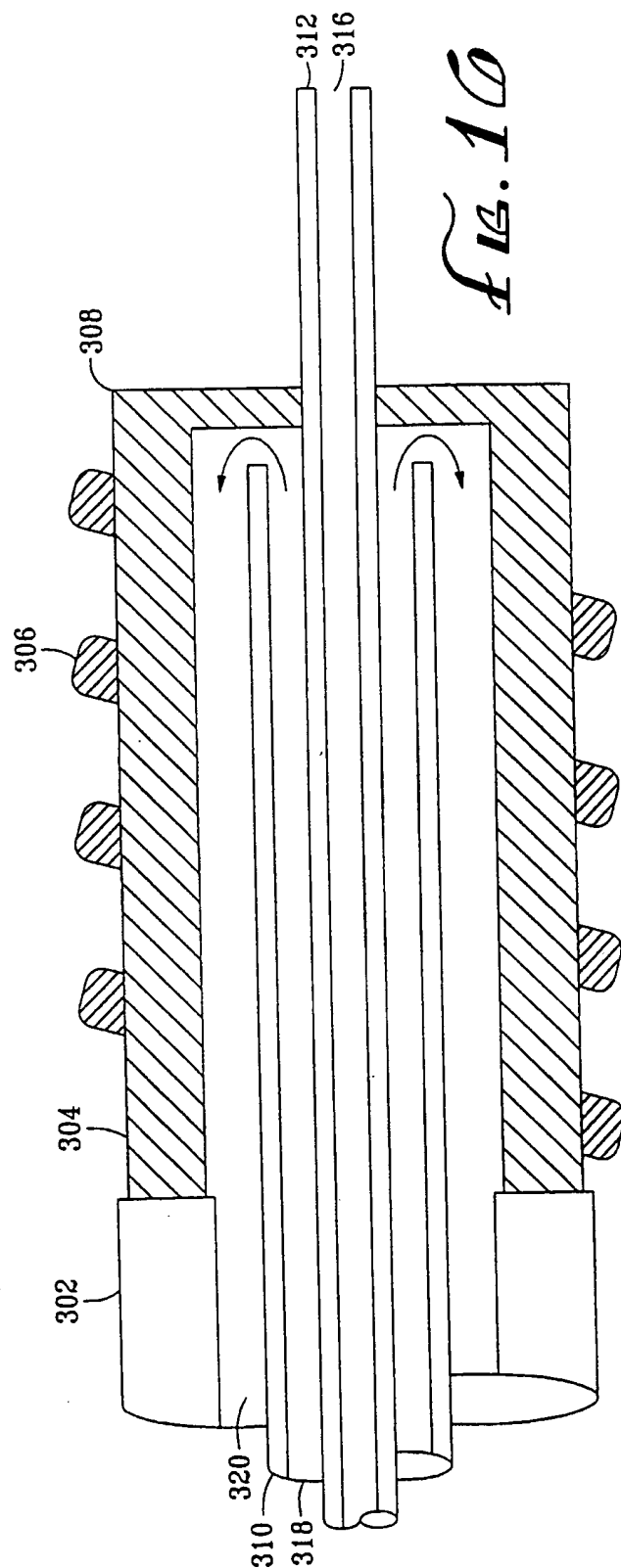


Fig. 10

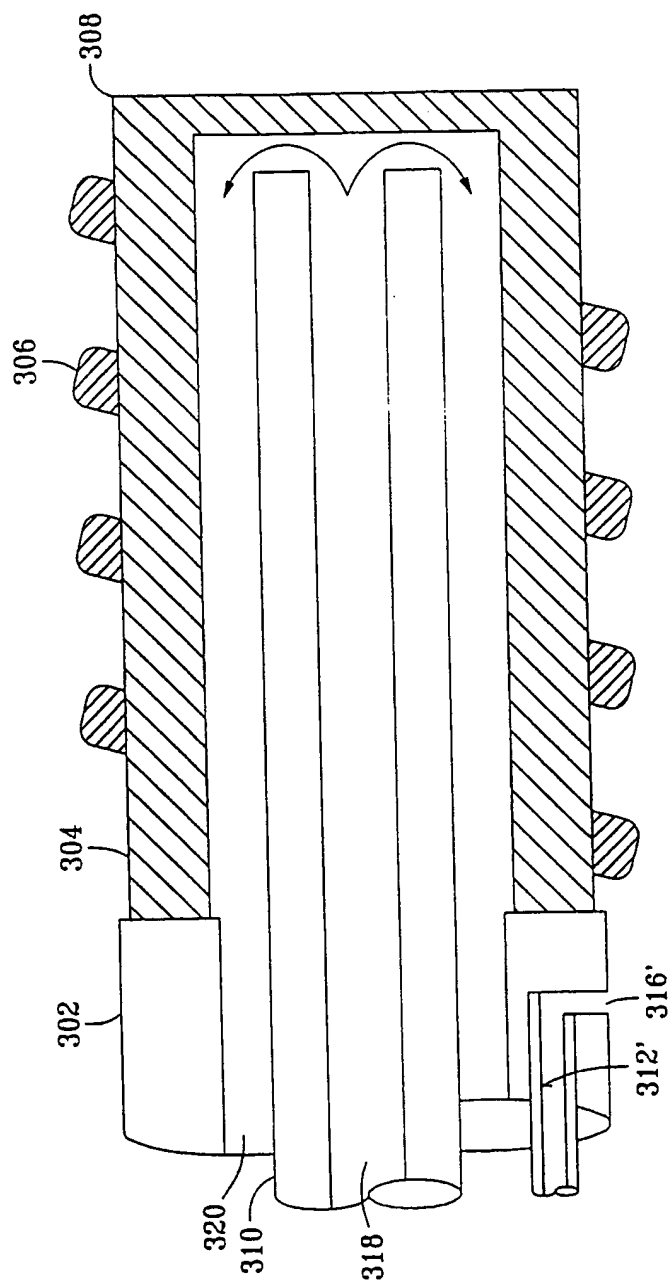


FIG. 17

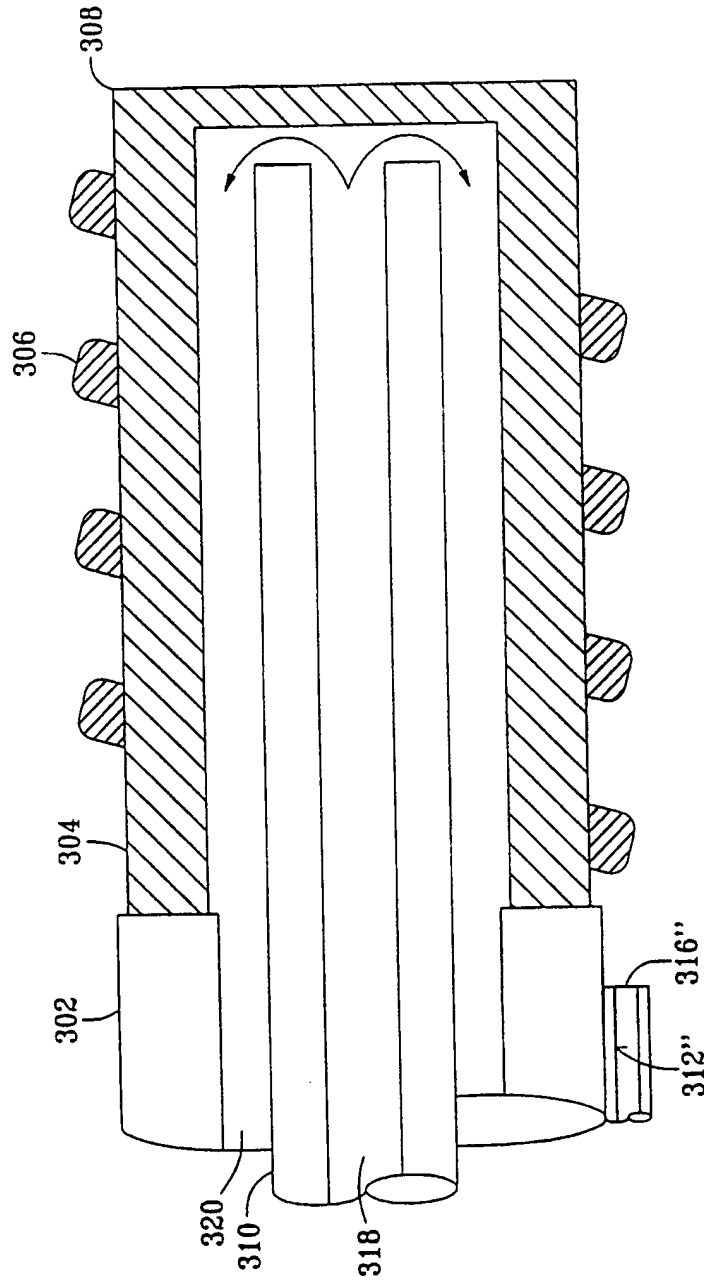


FIG. 18

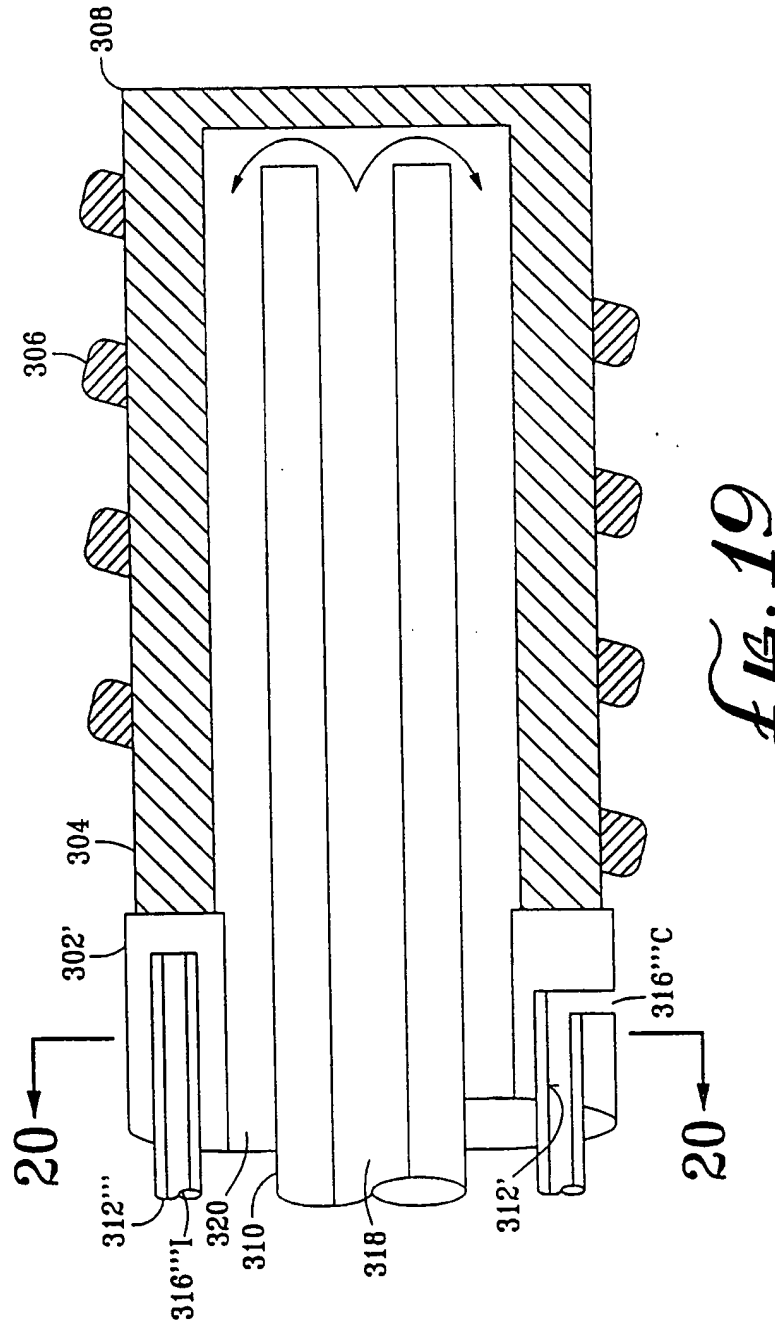


Fig. 19

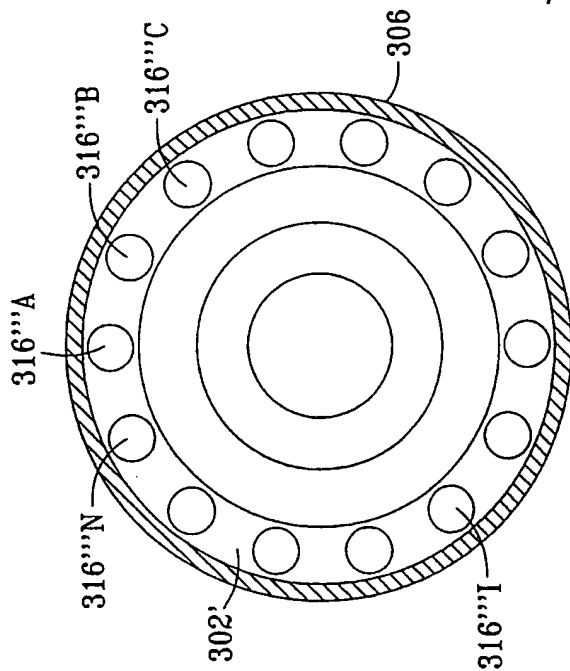
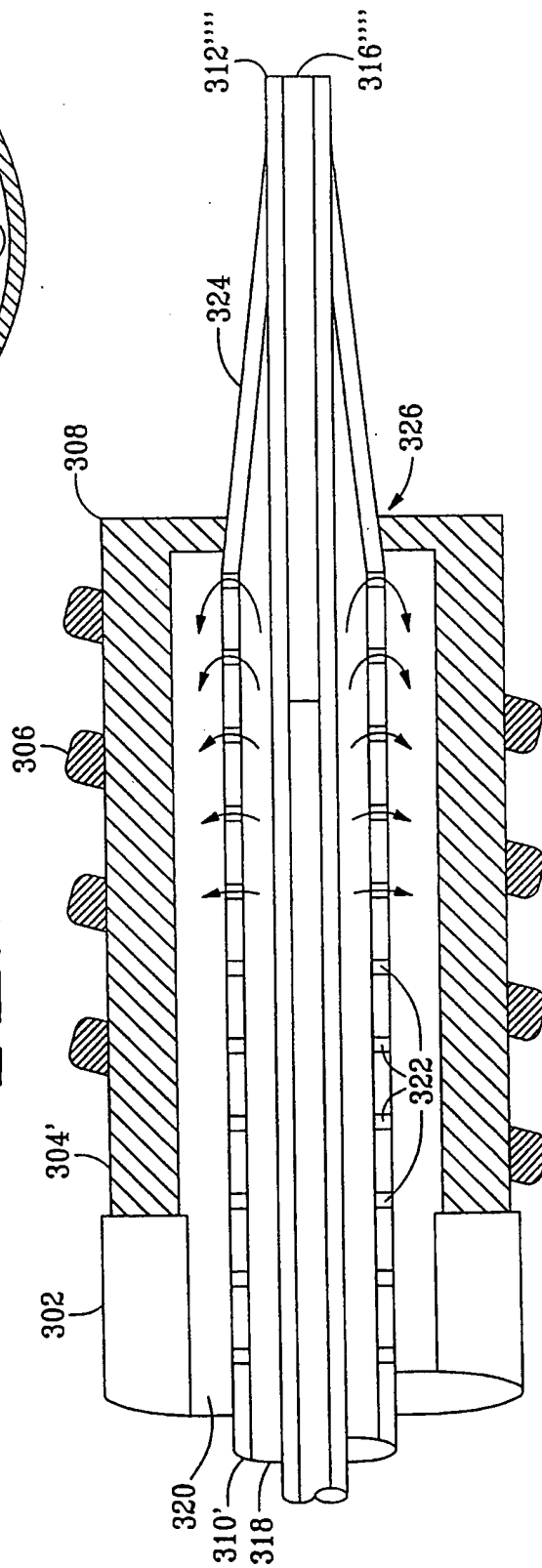


FIG. 20

FIG. 21



INTERNATIONAL SEARCH REPORT

International Application No

PC1/US 99/14257

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61M1/36 A61F7/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61M A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 624 392 A (SAAB MARK A) 29 April 1997 (1997-04-29) column 7, line 63 -column 10, line 10; figures 1,3,6 column 13, line 22 -column 14, line 14 ---	1-3, 6-11,15
X	WO 91 05528 A (GRANULAB B V) 2 May 1991 (1991-05-02) page 2, line 25 -page 4, line 8; figures 1,2 ---	1-5,7-10
A	US 3 425 419 A (DATO ANGELO ACTIS) 4 February 1969 (1969-02-04) cited in the application column 2, line 60 -column 3, line 16; figure 1 --- -/--	1,10,11

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

29 September 1999

Date of mailing of the international search report

05/10/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Zeinstra, H

INTERNATIONAL SEARCH REPORT

Inte rnal Application No
PCT/US 99/14257

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 486 208 A (GINSBURG ROBERT) 23 January 1996 (1996-01-23) column 5, line 37 -column 6, line 33; figures 5-9 ---	1,10,11
P,X	WO 98 26831 A (RADIANT MEDICAL) 25 June 1998 (1998-06-25) column 9, line 37 -column 10, line 19; figures 3,4 -----	1-4,8,9

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/14257

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5624392 A	29-04-1997	US 5342301 A	30-08-1994
		US 5411477 A	02-05-1995
		US 5902268 A	11-05-1999
		US 5569195 A	29-10-1996
		AU 7773891 A	10-12-1991
		CA 2082805 A	12-11-1991
		EP 0527969 A	24-02-1995
		WO 9117788 A	28-11-1991
WO 9105528 A	02-05-1991	NONE	
US 3425419 A	04-02-1969	NONE	
US 5486208 A	23-01-1996	US 5837003 A	17-11-1998
WO 9826831 A	25-06-1998	AU 5901398 A	15-07-1998